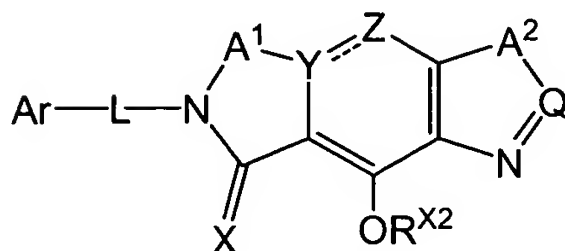


Claims

1. (twice amended): A compound having the structure:

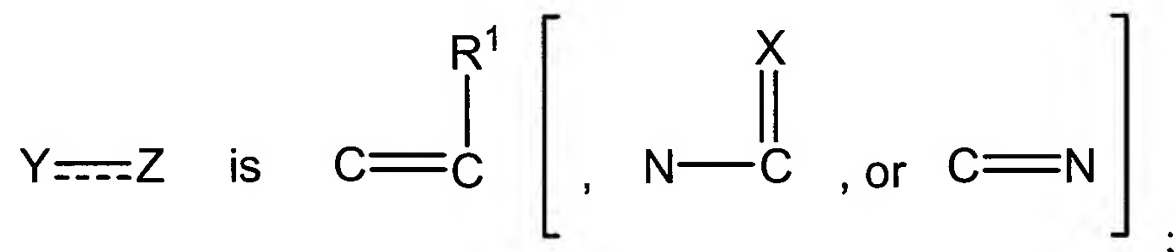


wherein:

A^1 [and A^2 are] is independently selected from [O, S, NR,] $C(R^2)_2$, CR^2OR , $CR^2OC(=O)R$, $C(=O)$, $C(=S)$, CR^2SR , and $C(=NR)$,

A^2 is independently selected from $C(R^2)_2-C(R^3)_2$, $C(R^2)=C(R^3)$, $[C(R^2)_2-O, NR-C(R^3)_2, N=C(R^3), N=N, SO_2-NR,]$ and $C(=O)C(R^3)_2$, $[C(=O)NR, C(R^2)_2-C(R^3)_2-C(R^3)_2, C(R^2)=C(R^3)-C(R^3)_2, C(R^2)C(=O)NR, C(R^2)C(=S)NR, C(R^2)=N-C(R^3)_2, C(R^2)=N-NR, and N=C(R^3)-NR]$;

Q is [N, ^+NR , or] CR^4 ;



L is selected from a bond, O, S, S-S, S(=O), S(=O)₂, S(=O)₂NR, NR, N-OR, C₁-C₁₂ alkylene, C₁-C₁₂ substituted alkylene, C₂-C₁₂ alkenylene, C₂-C₁₂ substituted alkenylene, C₂-C₁₂ alkynylene, C₂-C₁₂ substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), C(=O)NH(CH₂)_n, or (CH₂CH₂O)_n, where n [may be] is optionally 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N-OR, N-NR₂, N-CR₂OR and N-CR₂NR₂;

Ar is selected from (a) a C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

[R¹,] R², R³ and R⁴ are each independently selected from H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7

membered ring sultam, C₁–C₈ alkylsulfonate, C₁–C₈ alkylamino, 4-dialkylaminopyridinium, C₁–C₈ alkylhydroxyl, C₁–C₈ alkylthiol, –SO₂R, –SO₂Ar, –SOAr, –SAr, –SO₂NR₂, –SOR, –CO₂R, –C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, –CN, –N₃, –NO₂, C₁–C₈ alkoxy, C₁–C₈ trifluoroalkyl, C₁–C₈ alkyl, C₁–C₈ substituted alkyl, C₃–C₁₂ carbocycle, C₃–C₁₂ substituted carbocycle, C₆–C₂₀ aryl, C₆–C₂₀ substituted aryl, C₂–C₂₀ heteroaryl, and C₂–C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two R² or two R³ may form a spiro ring; [and]

R¹ is independently selected from CR₃, NRSO₂R, OC(=O)NR₂, OC(=O)R, SR, H, F, Cl, Br, I, OH, –NH₂, –NH₃⁺, –NHR, –NR₂, –NR₃⁺, C₁–C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁–C₈ alkylsulfonate, C₁–C₈ alkylamino, 4-dialkylaminopyridinium, C₁–C₈ alkylhydroxyl, C₁–C₈ alkylthiol, –SO₂R, –SO₂Ar, –SOAr, –SAr, –SO₂NR₂, –SOR, –CO₂R, –C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, –CN, –N₃, –NO₂, C₁–C₈ alkoxy, C₁–C₈ trifluoroalkyl, C₁–C₈ alkyl, C₁–C₈ substituted alkyl, C₃–C₁₂ carbocycle, C₃–C₁₂ substituted carbocycle, C₆–C₂₀ aryl, C₆–C₂₀ substituted aryl, C₂–C₂₀ heteroaryl, and C₂–C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

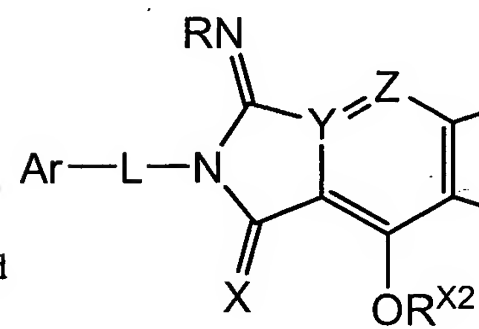
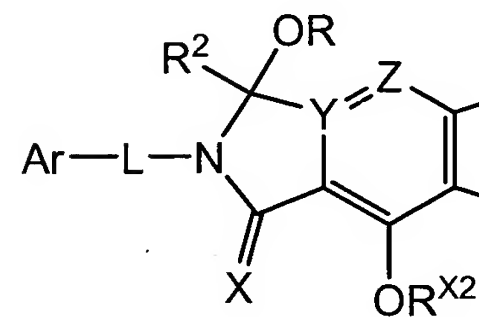
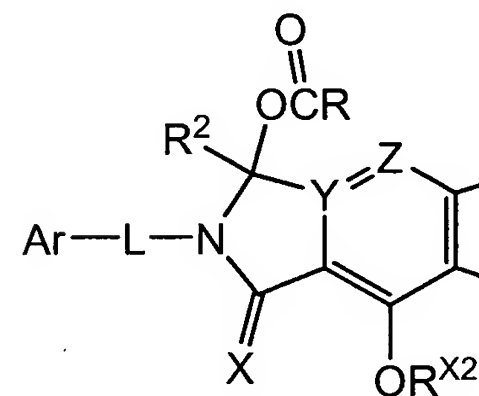
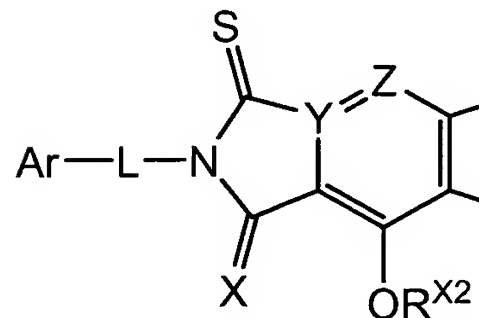
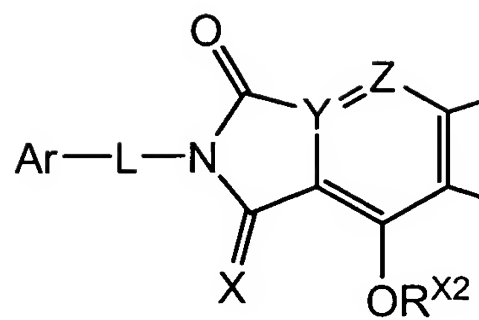
R is independently selected from H, C₁–C₈ alkyl, C₁–C₈ substituted alkyl, C₆–C₂₀ aryl, C₆–C₂₀ substituted aryl, C₂–C₂₀ heteroaryl, and C₂–C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

R^{X2} is independently selected from H, C₁–C₈ alkyl, C₁–C₈ substituted alkyl, C₆–C₂₀ aryl, C₆–C₂₀ substituted aryl, C₂–C₂₀ heteroaryl, and C₂–C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, [a prodrug, a pharmaceutically acceptable prodrug,] a prodrug moiety, and a protecting group[, and a phosphonate prodrug moiety];

and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof;

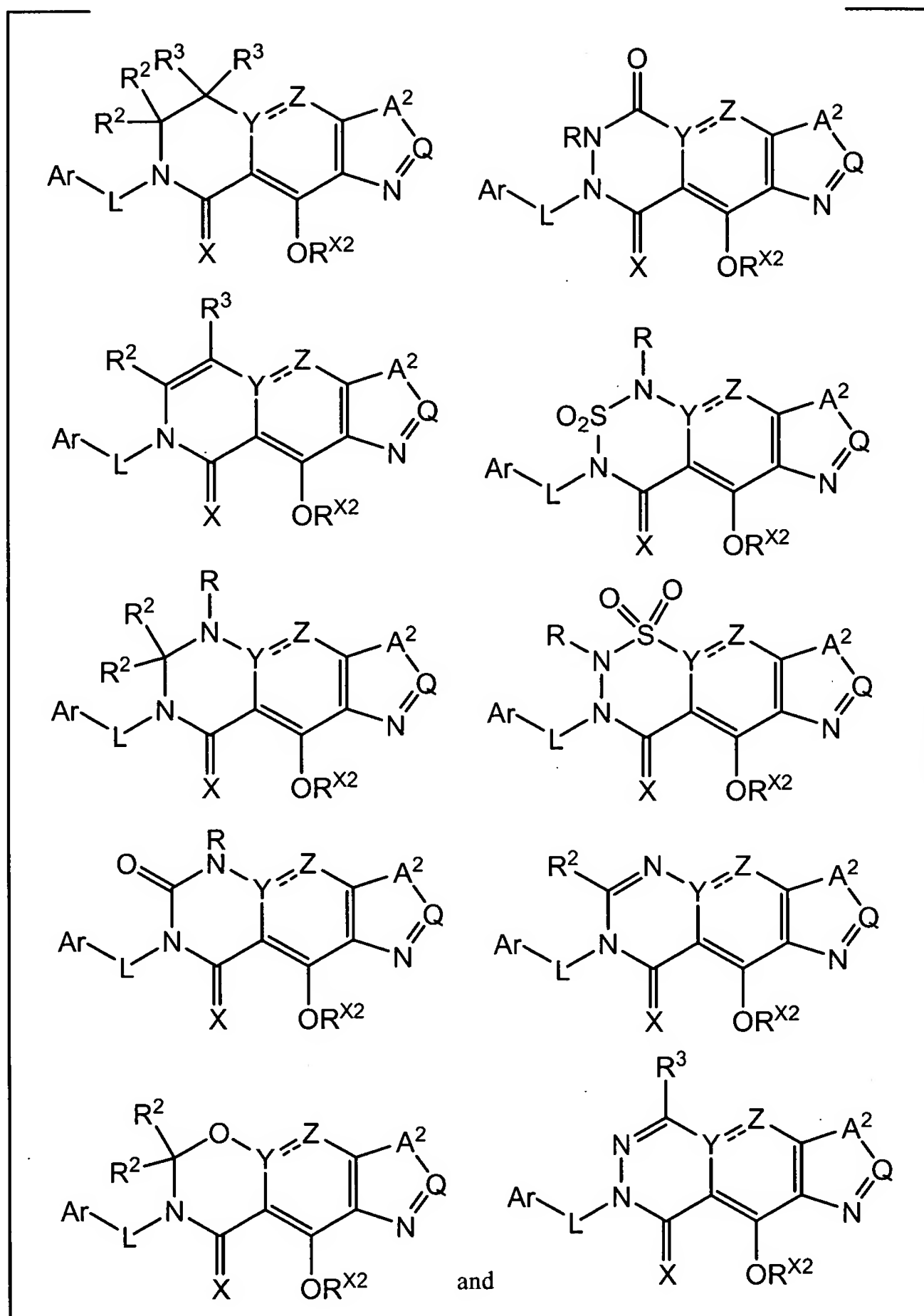
with the proviso that when Y=Z is C=C(OH), X is O, A¹ is C(=O), A² is C(R²)=C(R³), and Q is CH, then L is not a bond.

2. (once amended): A compound of claim 1 selected from the structures:

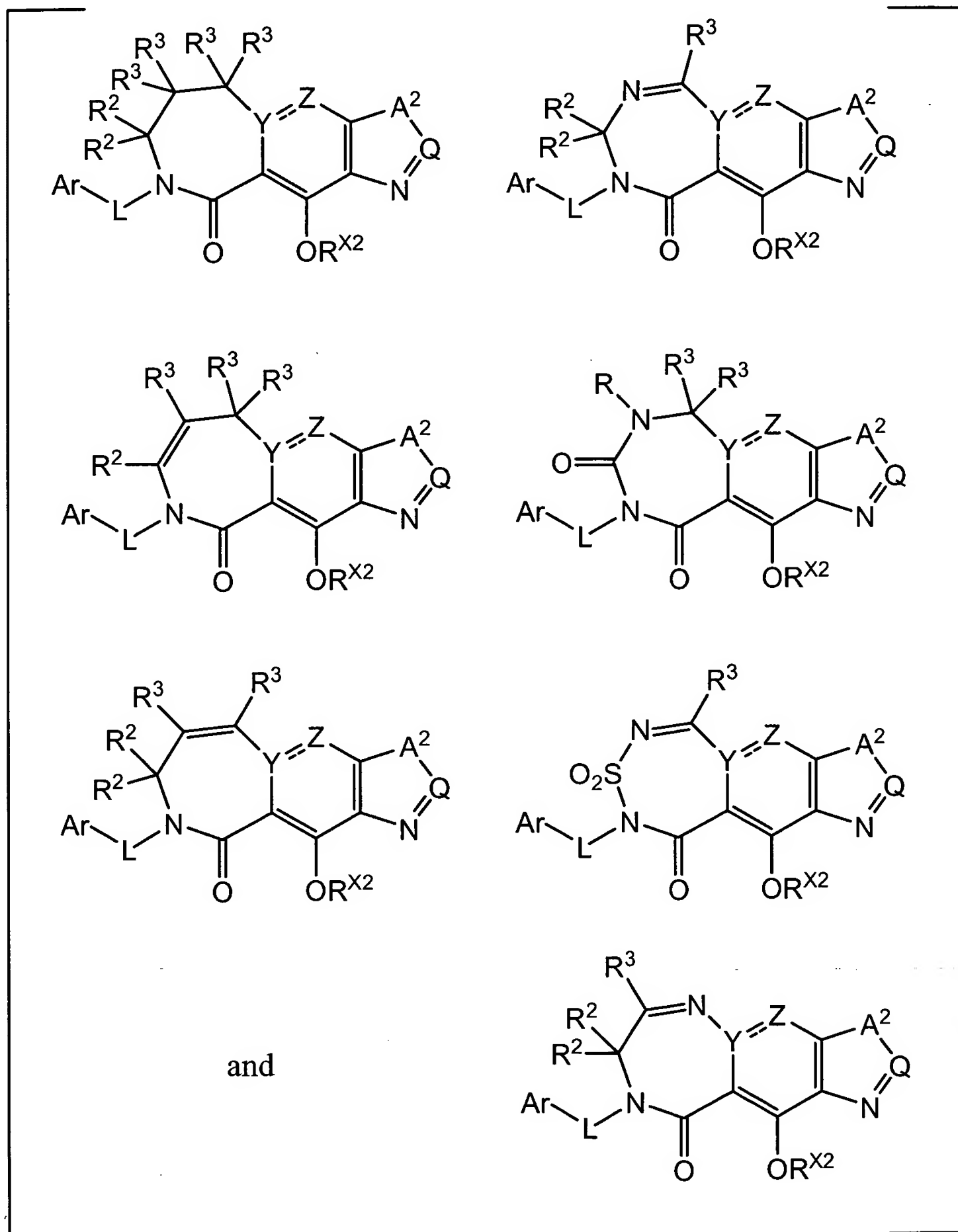


and

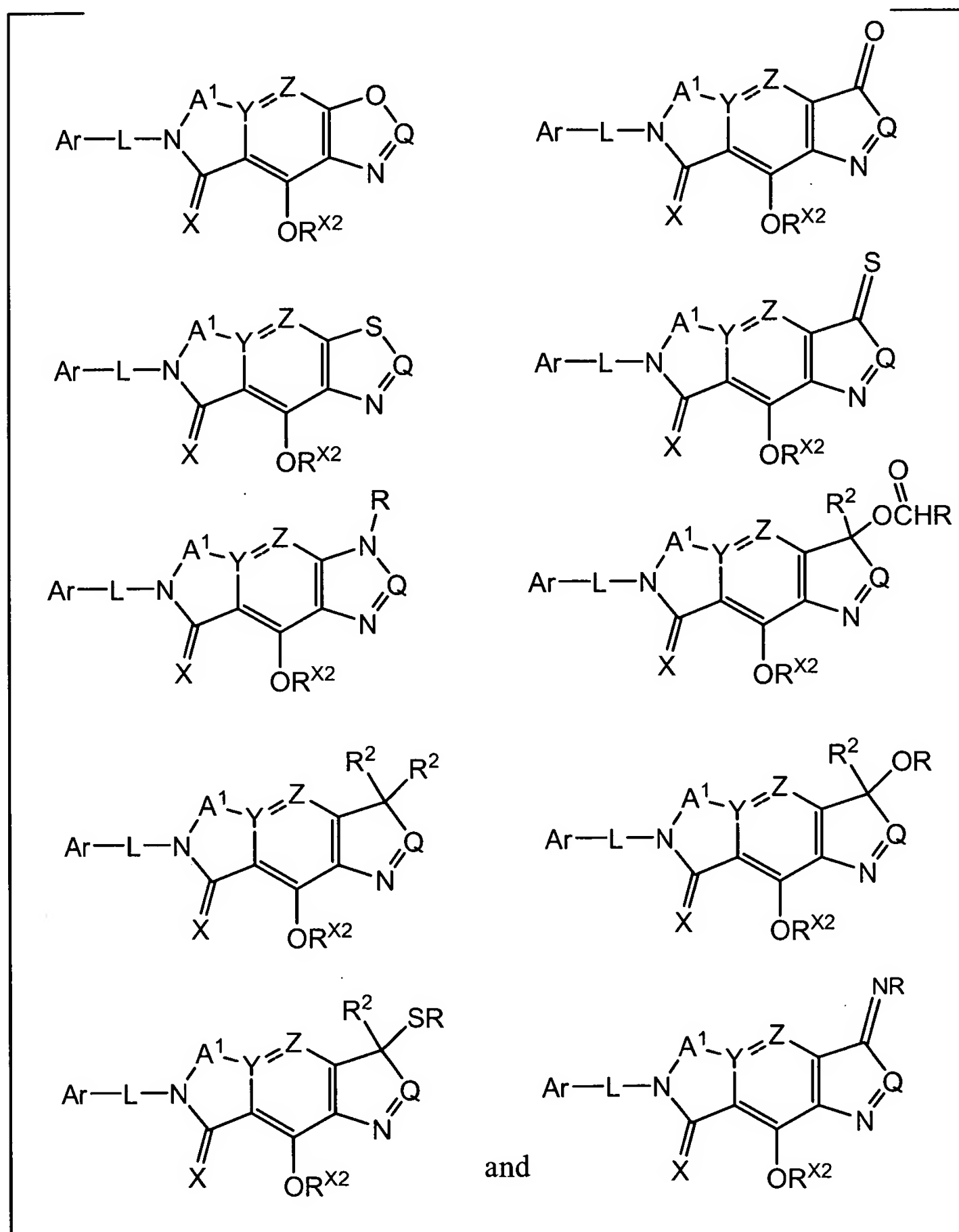
3. (once amended): A compound of claim 1 [selected from the structures:] wherein
A¹ is CH₂.



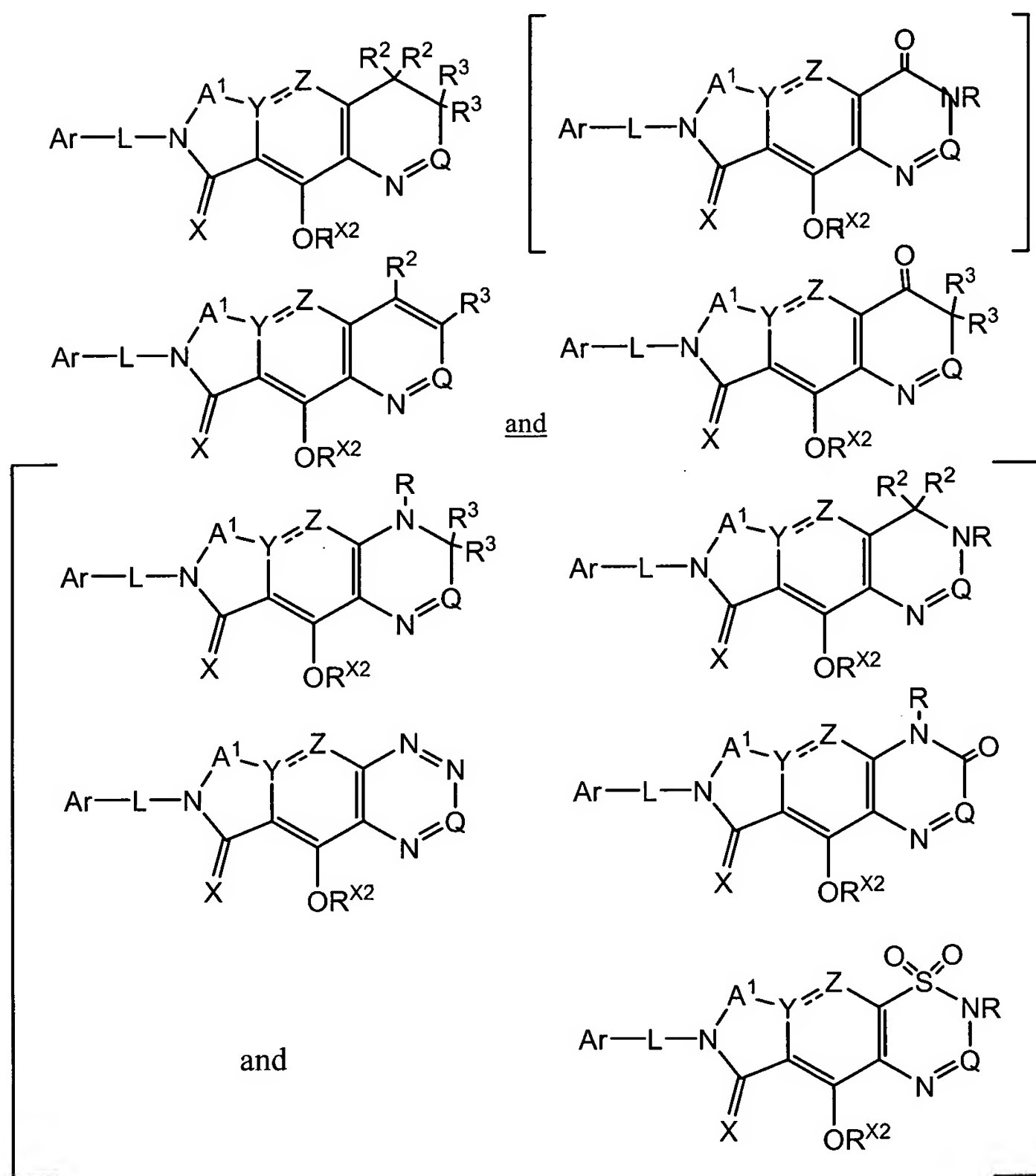
4. (once amended): A compound of claim 1 [selected from the structures:] wherein
Ar is a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic
carbocycle or heterocycle containing 3 to 12 ring atoms.



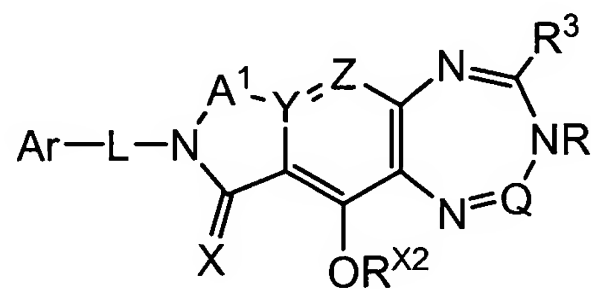
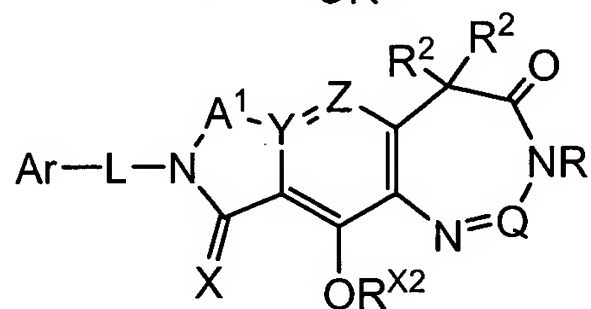
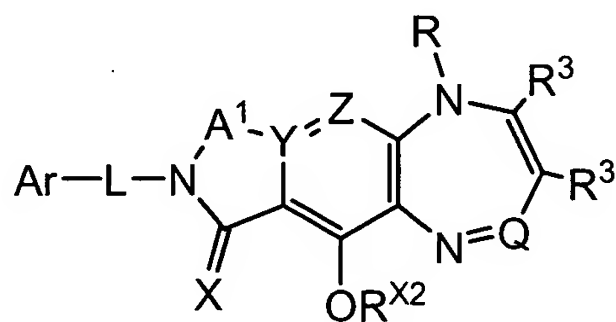
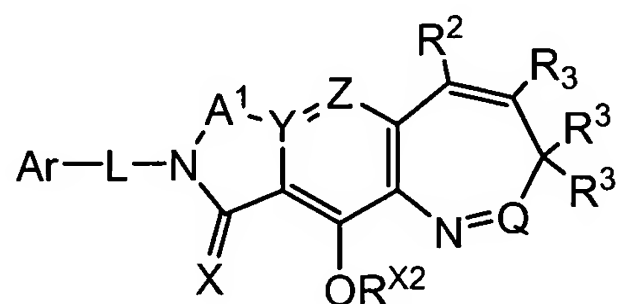
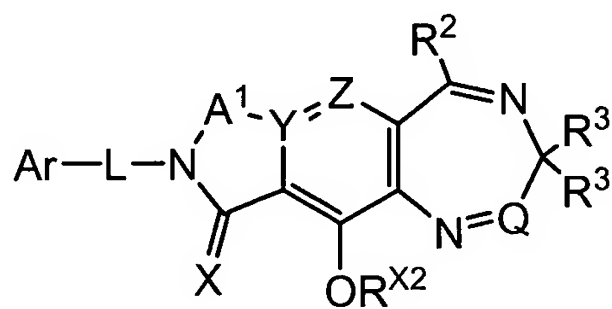
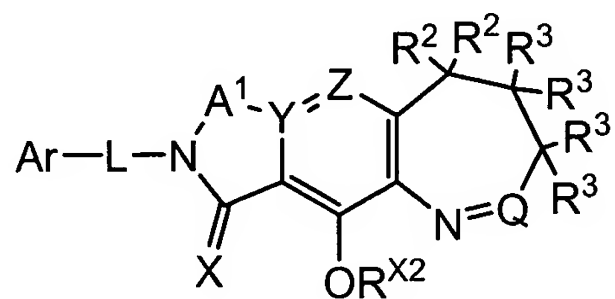
5. (once amended): A compound of claim 1 [selected from the structures:] wherein
R¹ is selected from R, OR, NR₂, NHR, NHSO₂R and NRSO₂R;



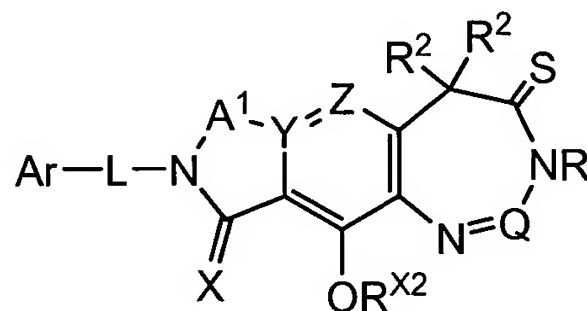
6. (once amended): A compound of claim 1 selected from the structures:



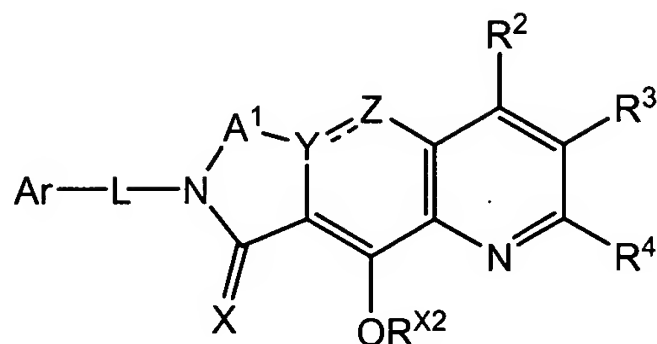
7. (once amended): A compound of claim 1 [selected from the structures:] wherein R^{x2} is a protecting group selected from the group consisting of benzyhydryl (CHPh_2), trialkylsilyl (R_3Si), 2-trimethylsiloxyethyl, alkoxymethyl (CH_2OR), and ester ($\text{C}(=\text{O})\text{R}$).



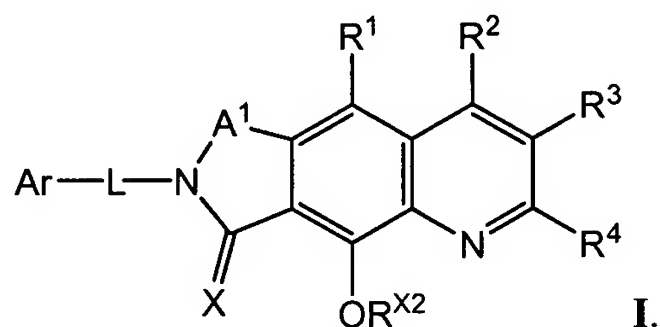
and



8. (once amended): A compound of claim [6] 1 having the structure:

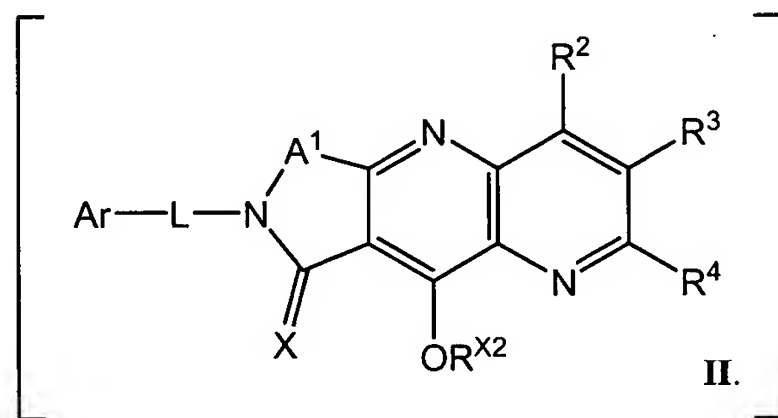


9. (once amended): A compound of claim [6] 1 having Formula I:

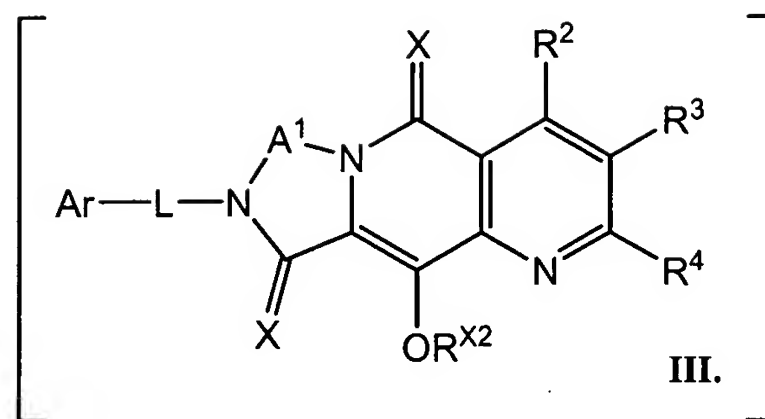


wherein R^{x2} is H and X is O.

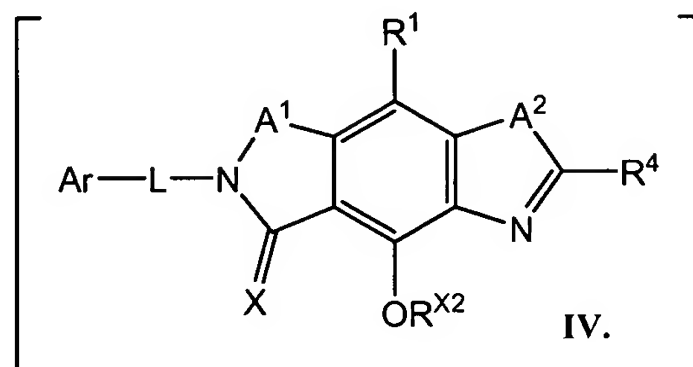
10. (once amended): A compound of claim [6 having Formula II:] 1 wherein L is not a bond.



11. (once amended): A compound of claim [6 having Formula III:] 1 wherein R⁴ is H.



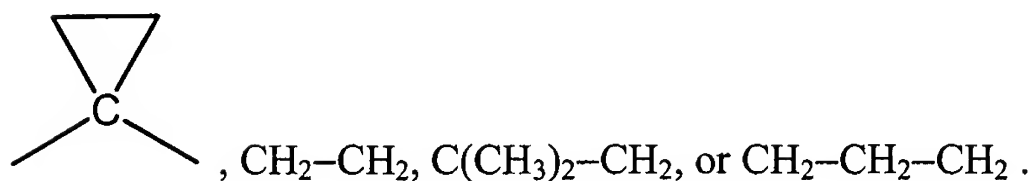
12. (once amended): A compound of claim 1 [having Formula IV:] wherein Ar is C₆ - C₂₀ substituted aryl.



13. (once amended): A compound of claim 1 having [comprising] at least one phosphonate group.

14. (previously presented): A compound of claim 1 wherein substituted alkyl, substituted alkylene, substituted alkyenylene, substituted alkynylene, substituted carbocycle, substituted aryl, and substituted heteroaryl are independently substituted with one or more substituents selected from F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₃-C₁₂ carbocycle, C₆-C₂₀ aryl, C₂-C₂₀ heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

15. (previously presented): The compound of claim 1 wherein A^1 is CH_2 , $C(CH_3)_2$,



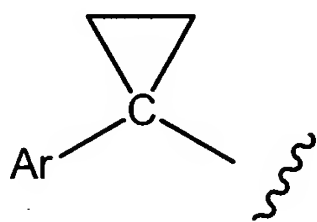
16. (previously presented): The compound of claim 9 wherein X is O; L is CH_2 ; and Ar is substituted phenyl.

17. (previously presented): The compound of claim 16 wherein Ar is 4-fluorophenyl.

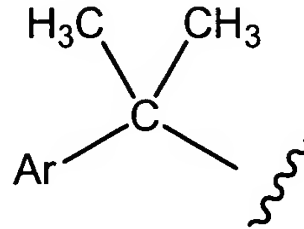
18. (previously presented): The compound of claim 9 wherein X is O; and R^2 , R^3 and R^4 are each H.

19. (previously presented): The compound of claim 9 wherein X is O; A^1 is CH_2 ; and R^2 , R^3 and R^4 are each H.

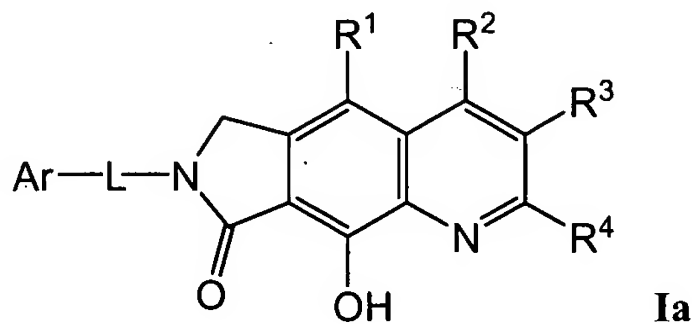
20. (previously presented): The compound of claim 1 wherein Ar-L is selected from the structures:

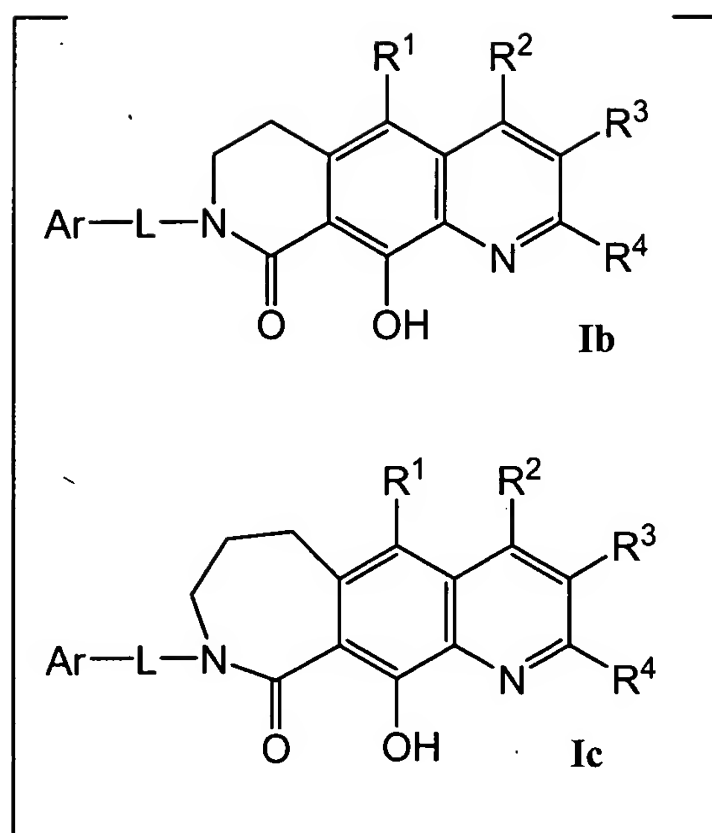


and

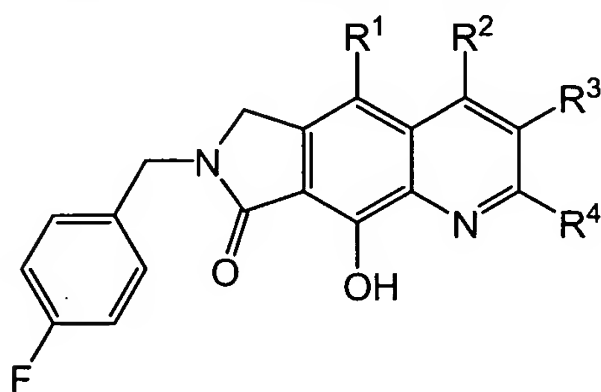


21. (once amended): A compound of claim 9 having [comprising] Formula Ia[, Ib, or Ic]:

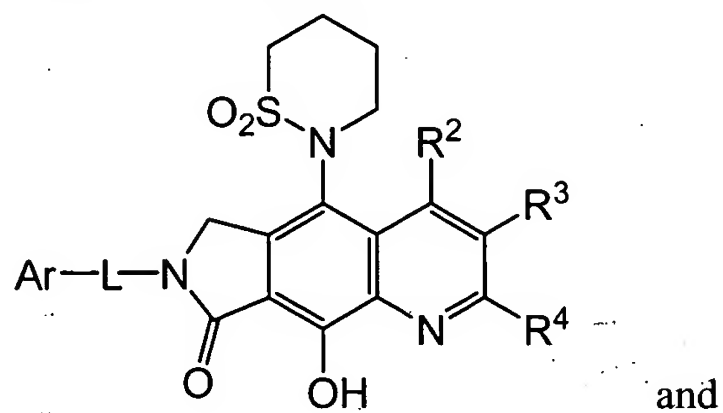


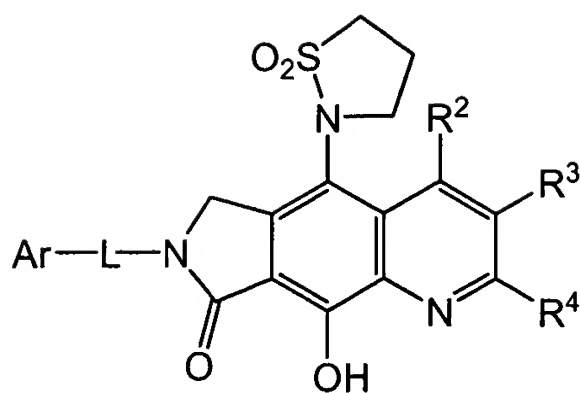


22. (previously presented): A compound of claim 9 having the structure:

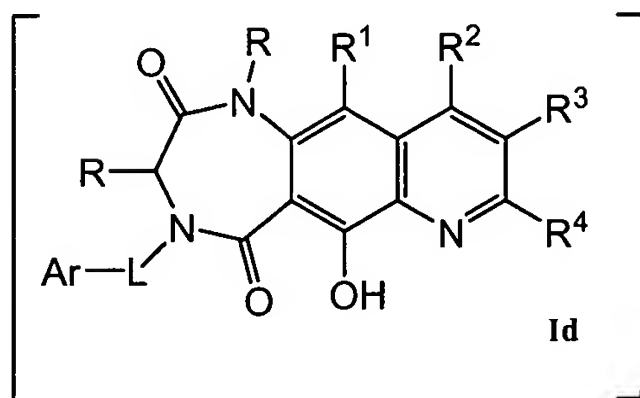


23. (previously presented): A compound of claim 22 selected from the structures:

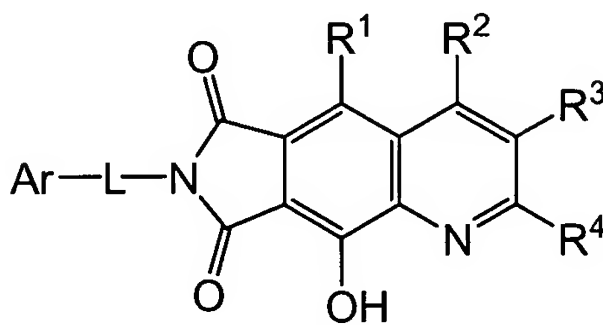




24. (once amended): A compound of claim 9 [having Formula Id:] wherein AR-L is para-fluorobenzyl.

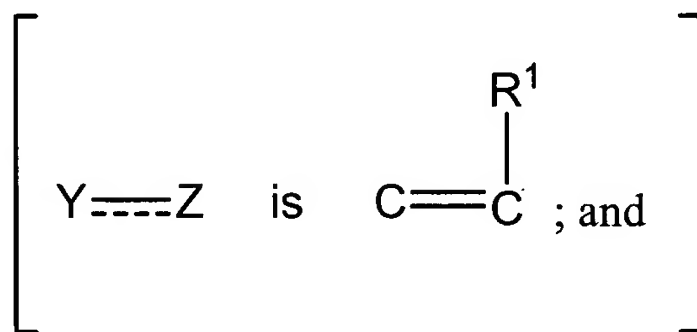


25. (previously presented): A compound of claim 9 having the structure:



with the proviso that when R¹ is OH, and R², R³, and R⁴ are H, then L is not a bond.

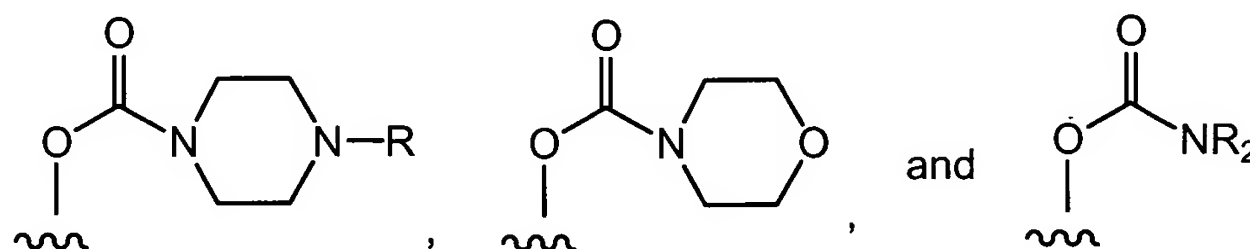
26. (once amended): A compound of claim 1 wherein



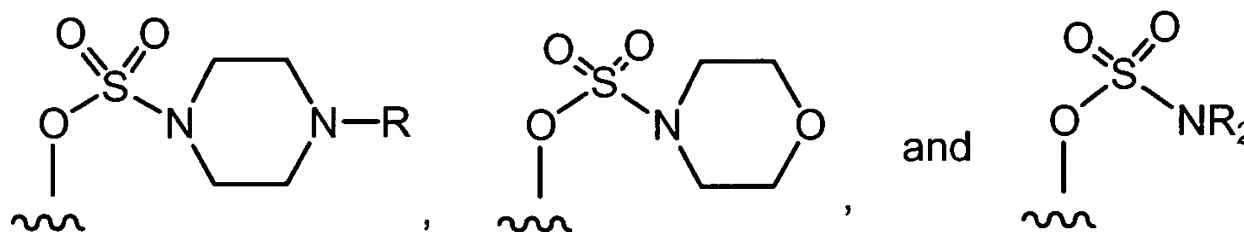
R^1 is selected from CR_3 , $C(=O)NR_2$, $OC(=O)OR$, $OC(=O)NR_2$, $OC(=O)R$, OSO_2NR_2 (sulfamate), NR_2 , $NRSO_2R$, SR , $S(O)R$, SO_2R and [or] SO_2NR_2 (sulfonamide).

27. (previously presented): The compound of claim 26 wherein at least one R is [comprises] a prodrug moiety.

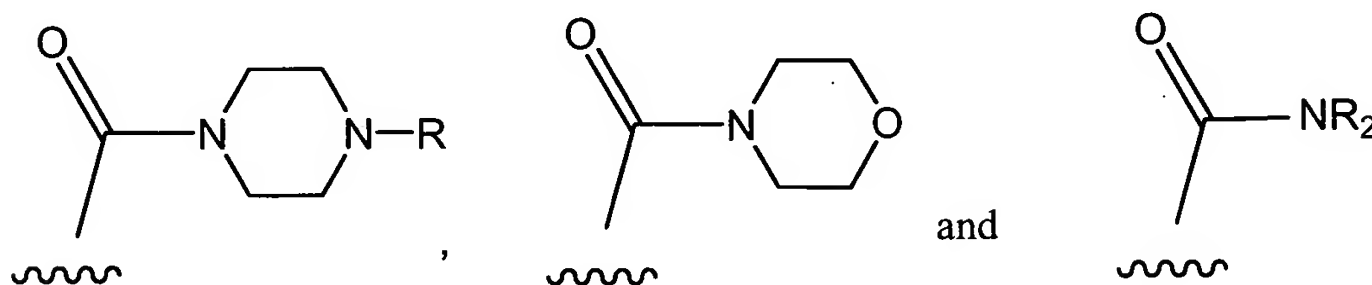
28. (previously presented): A compound of claim 1 wherein at least one of R^1 , R^2 , R^3 , and R^4 is selected from the structures:



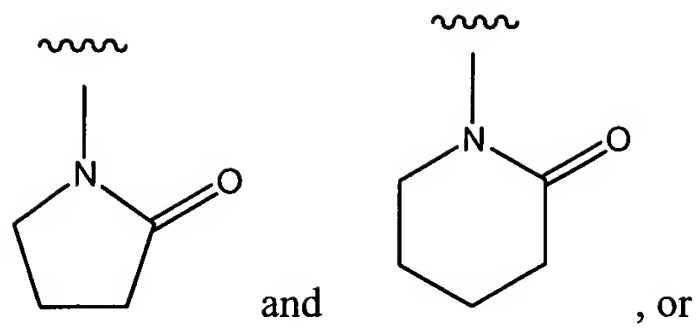
29. (previously presented): A compound of claim 1 wherein at least one of R^1 , R^2 , R^3 , and R^4 is selected from the structures:



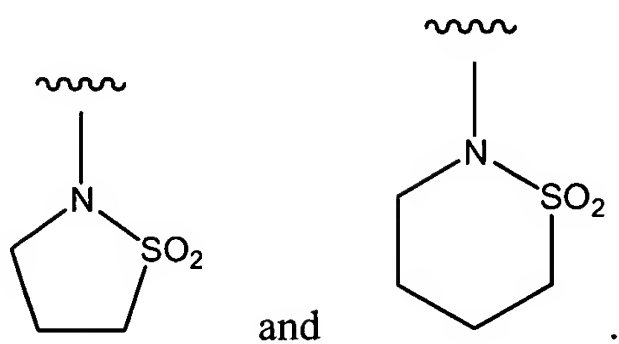
30. (previously presented): A compound of claim 1 wherein at least one of R^1 , R^2 , R^3 , and R^4 is selected from the structures:



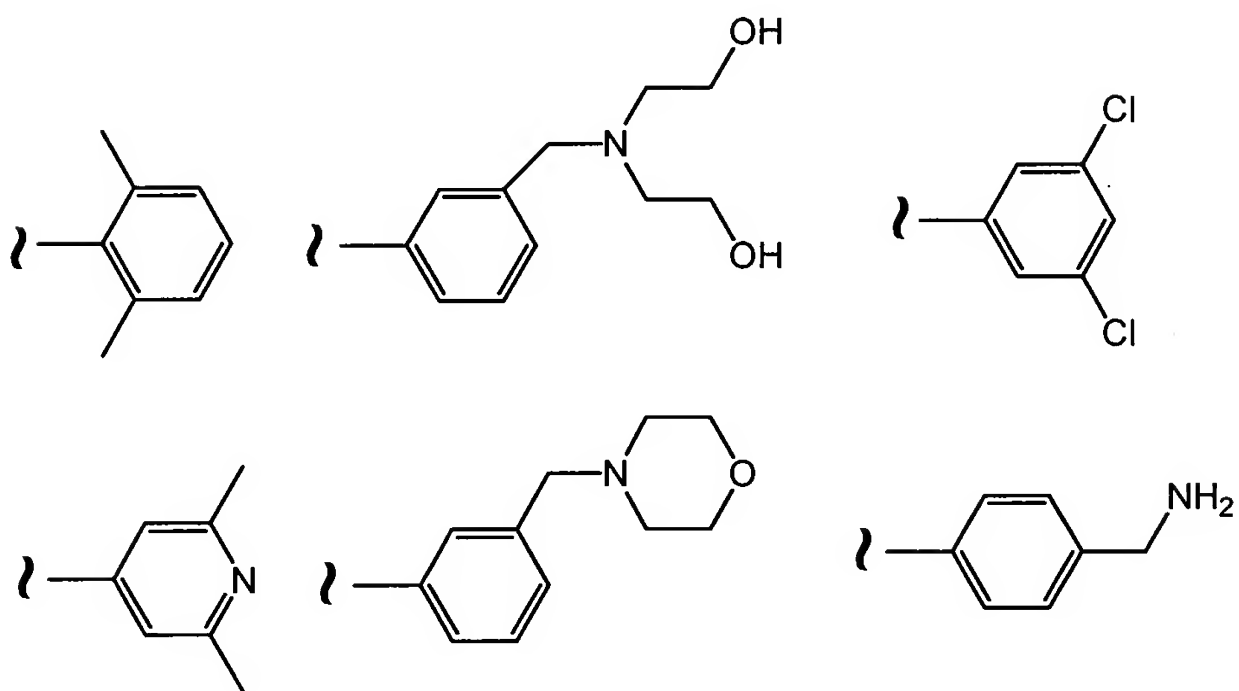
31. (previously presented): A compound of claim 1 wherein at least one of R^1 , R^2 , R^3 , and R^4 [comprise] is a lactam having the structures:

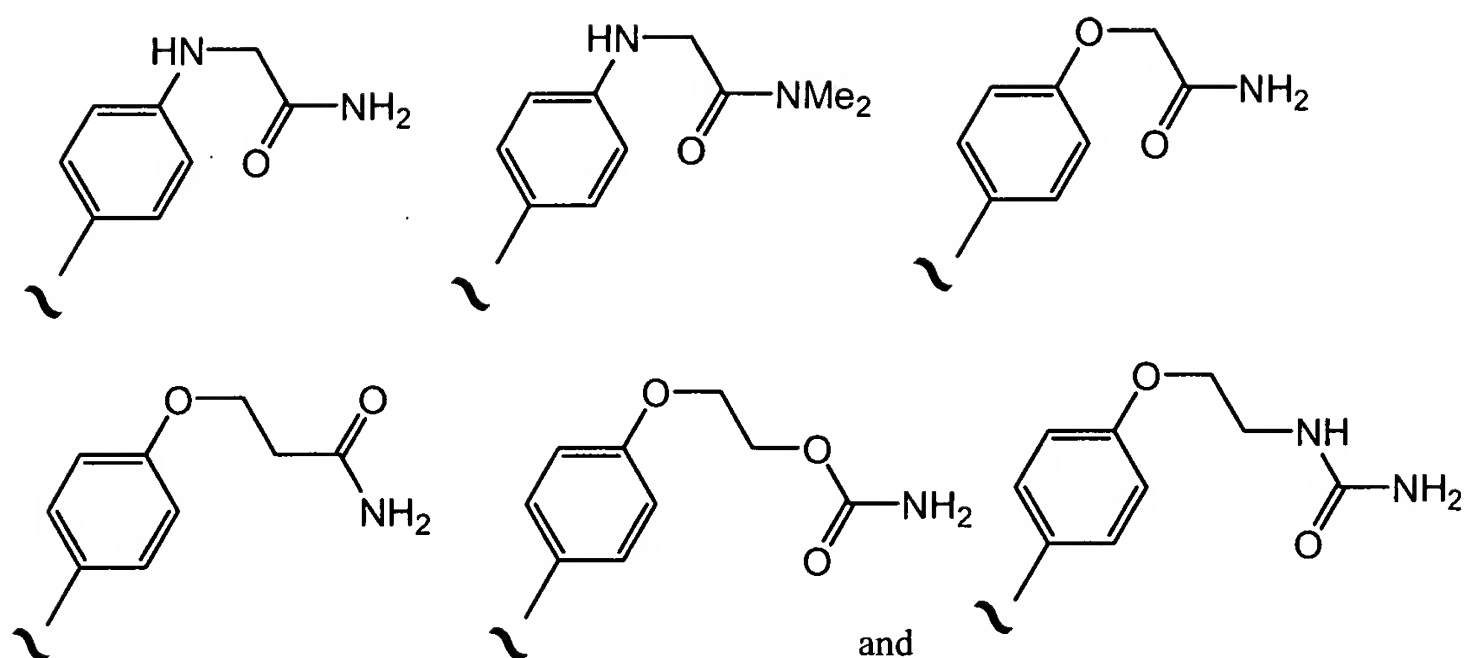



a sultam having the structures:



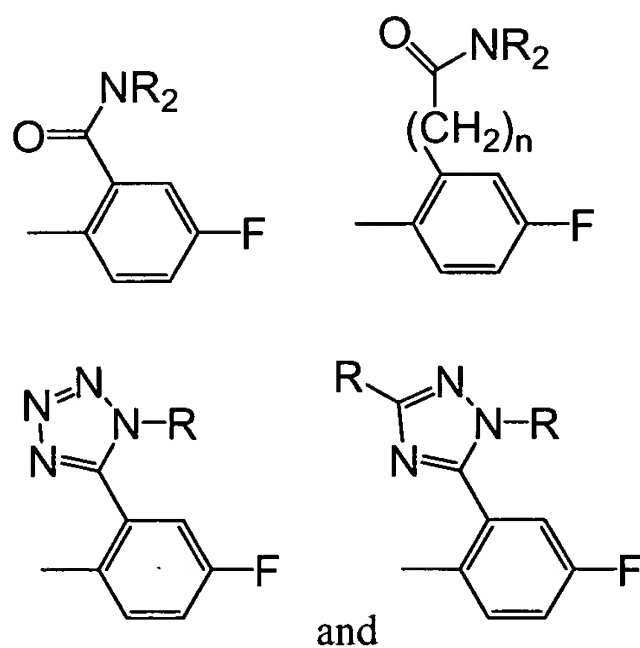
32. (previously presented): A compound of claim 1 wherein Ar is selected from the structures:





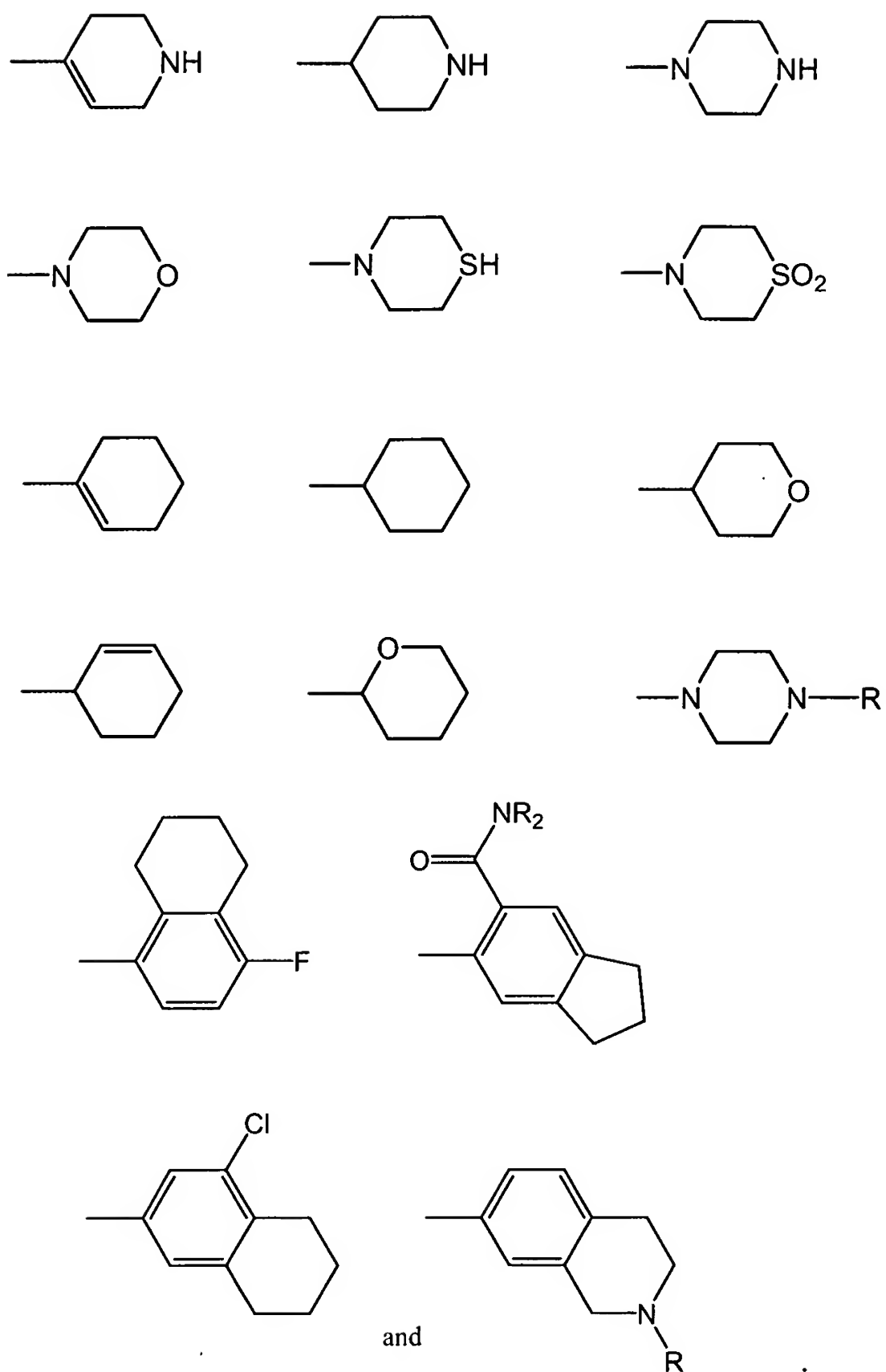
where the wavy line  indicates the covalent attachment site to L.

33. (previously presented): A compound of claim 1 wherein Ar is selected from the structures:

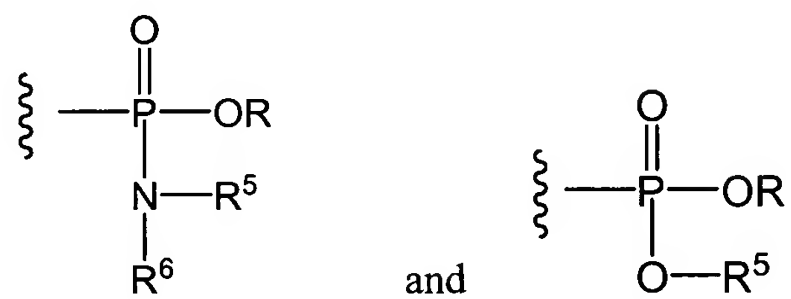


where n is 1 to 6.

34. (previously presented): A compound of claim 1 wherein Ar is selected from the structures:

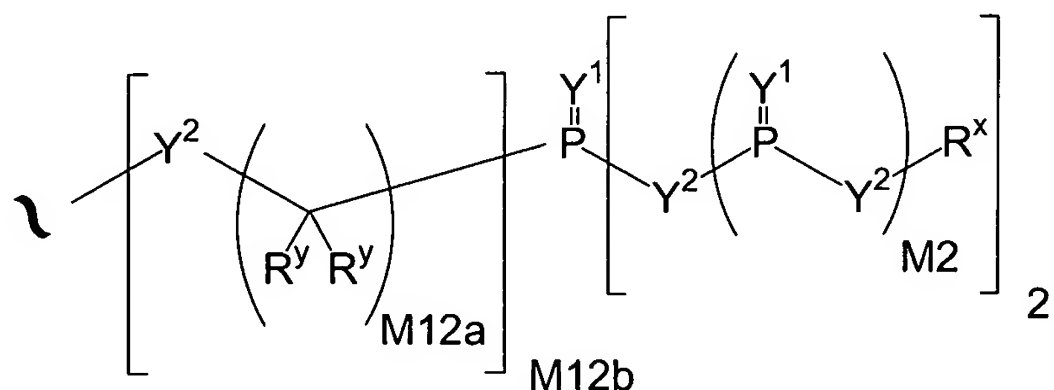


35. (previously presented): A compound of claim 1 comprising a prodrug moiety selected from the structures:



wherein R^5 is $-CR_2CO_2R^7$ where R^6 and R^7 are independently H or C_1-C_8 alkyl.

36. (previously presented): The compound of claim 1 comprising a phosphonate or prodrug moiety having the structure:



wherein:

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)_2)$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)_2)$, $-S(O)-$ (sulfoxide), $-S(O)_2-$ (sulfone), $-S-$ (sulfide), or $-S-S-$ (disulfide);

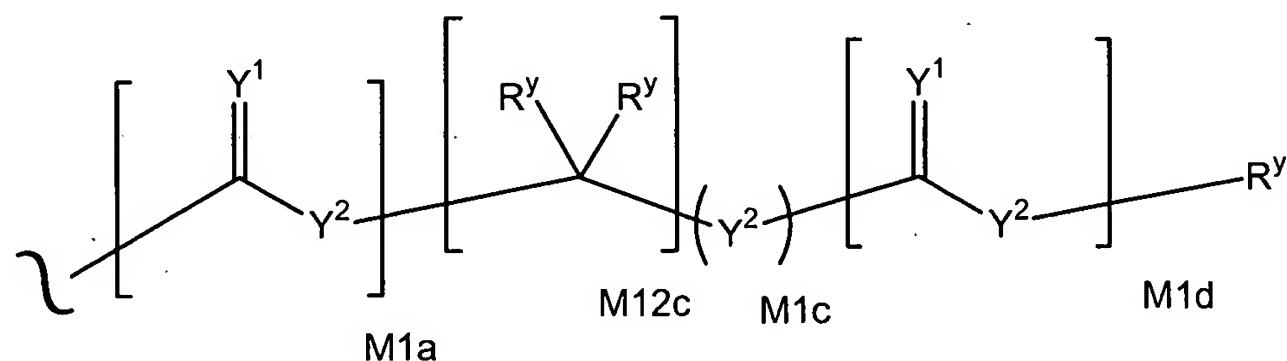
M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

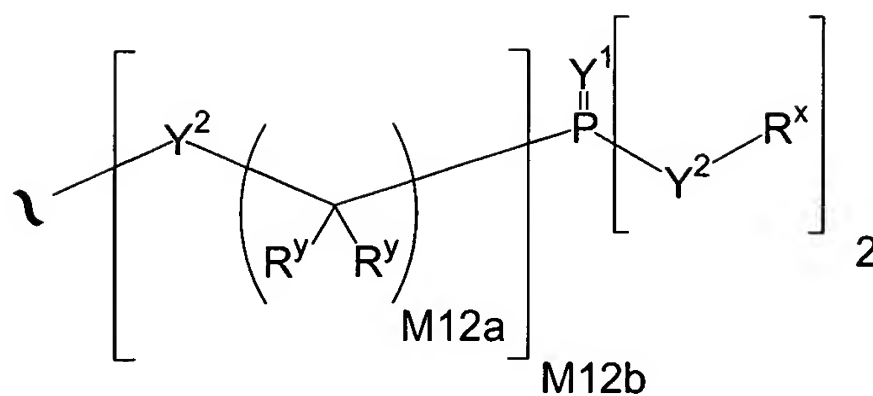
R^y is independently H, C_1-C_6 alkyl, C_1-C_6 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, or a protecting group, or where taken together at a carbon atom, two vicinal R^y groups form a carbocycle or a heterocycle; and

R^x is independently H, C_1-C_6 alkyl, C_1-C_6 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, or a protecting group, or the formula:

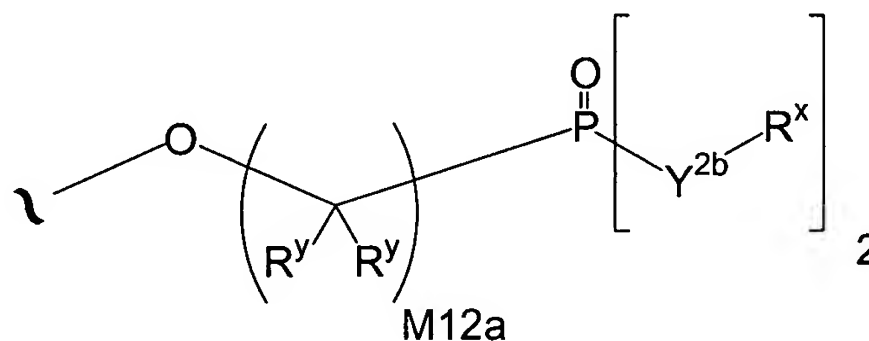


where M1a, M1c, and M1d are independently 0 or 1, and M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

37. (previously presented): The compound of claim 36 wherein the phosphonate or prodrug moiety has the structure:

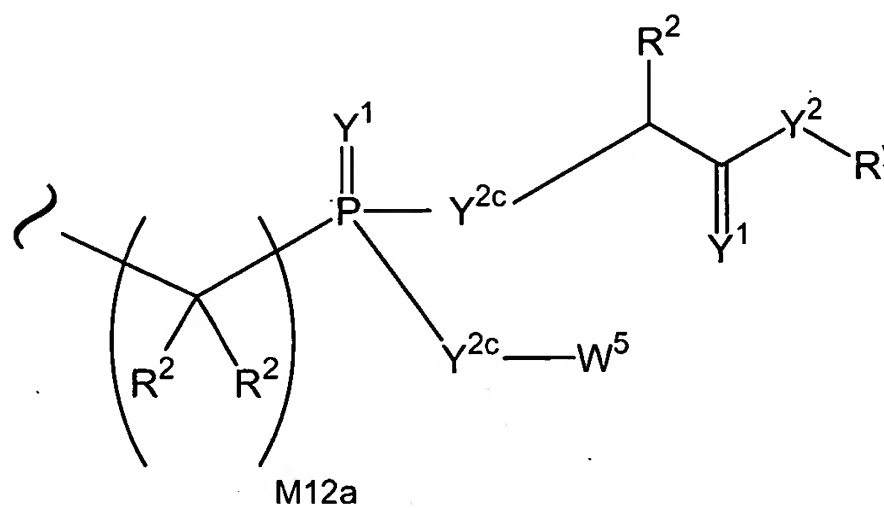


38. (previously presented): The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:



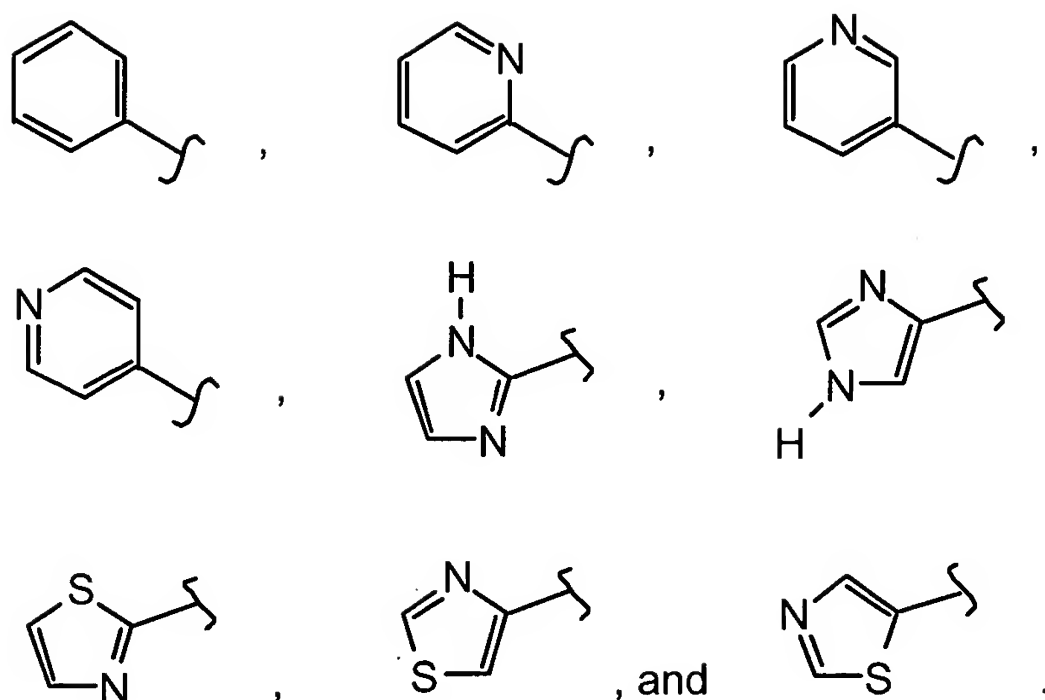
where Y^{2b} is O or $N(R^x)$.

39. (previously presented): The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:

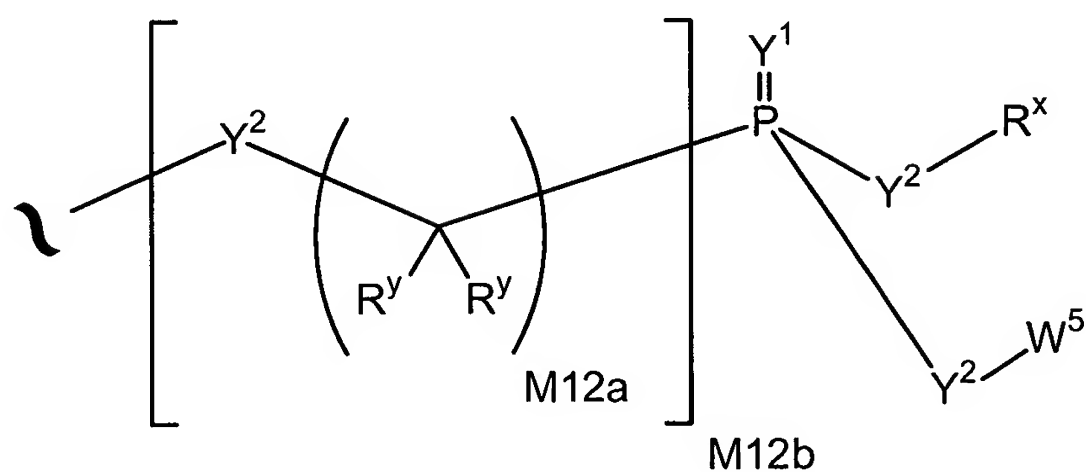


where W^5 is a carbocycle, and Y^{2c} is O, $N(R^y)$ or S.

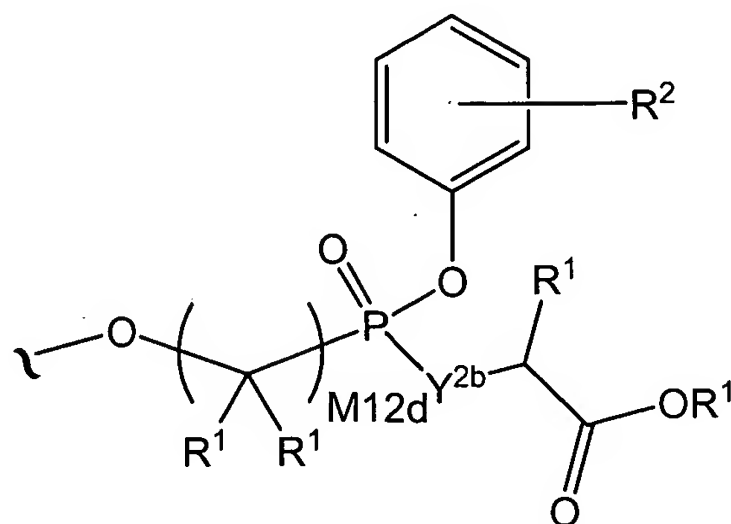
40. (previously presented): The compound of claim 39 wherein W^5 is selected from the structures:



41. (previously presented): The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:



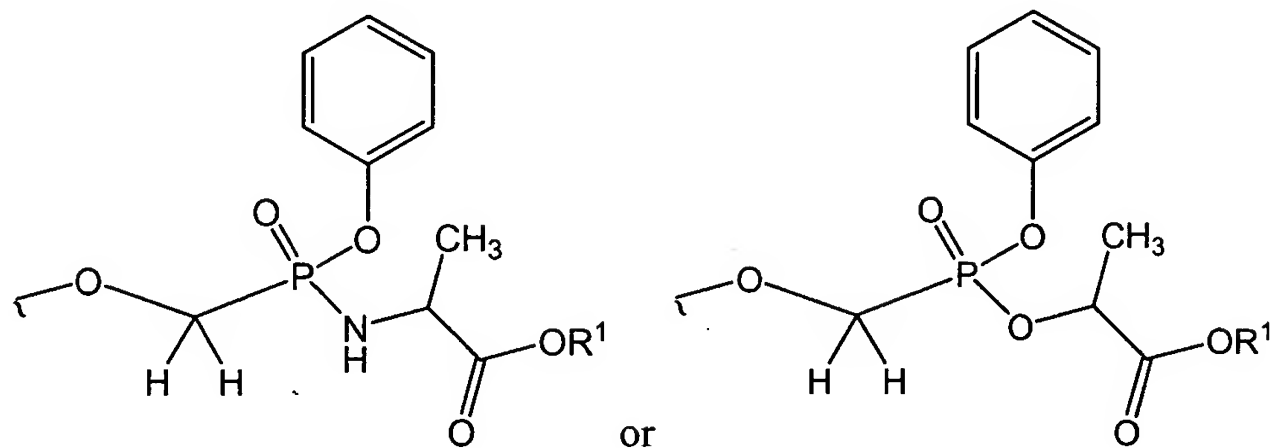
42. (once amended): The compound of claim 1 [41] wherein the phosphonate or prodrug moiety has the structure:



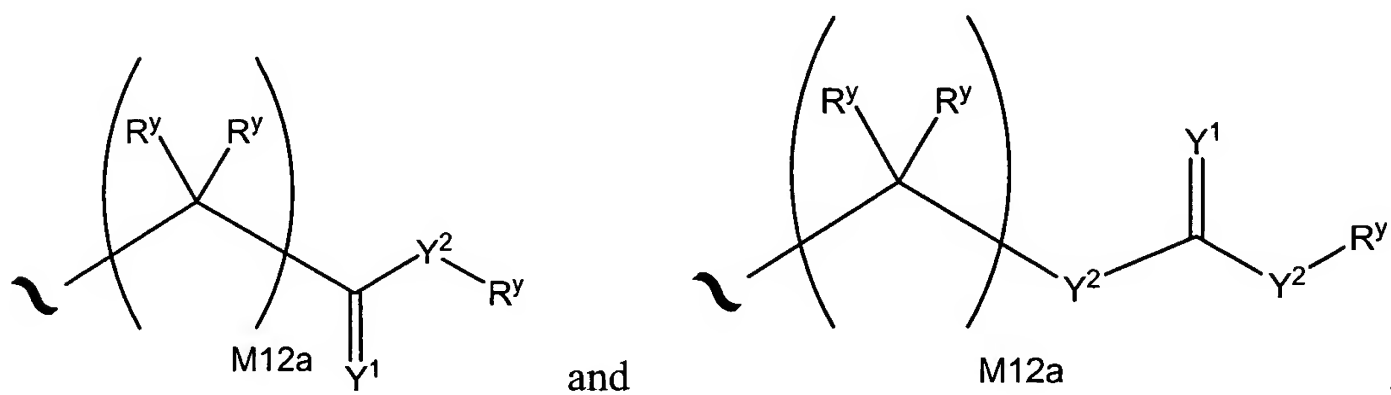
wherein Y^{2b} is O or $N(R^x)$; M12d is 1, 2, 3, 4, 5, 6, 7 or 8; R^1 is H or C_1-C_6 alkyl; and the phenyl carbocycle is substituted with 0 to 3 R^2 groups where R^2 is C_1-C_6 alkyl or substituted

alkyl.

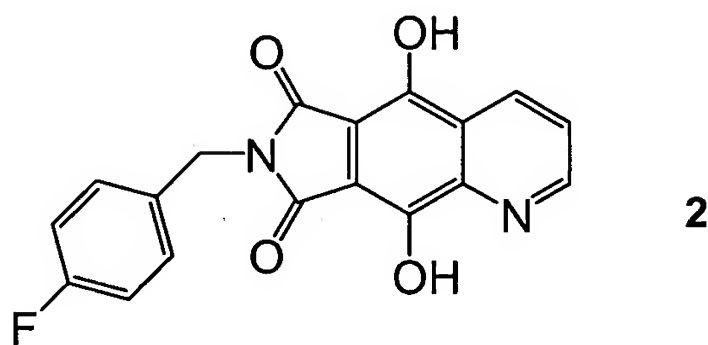
43. (once amended): The compound of claim 1 [42] wherein the phosphonate or prodrug moiety has the structure:



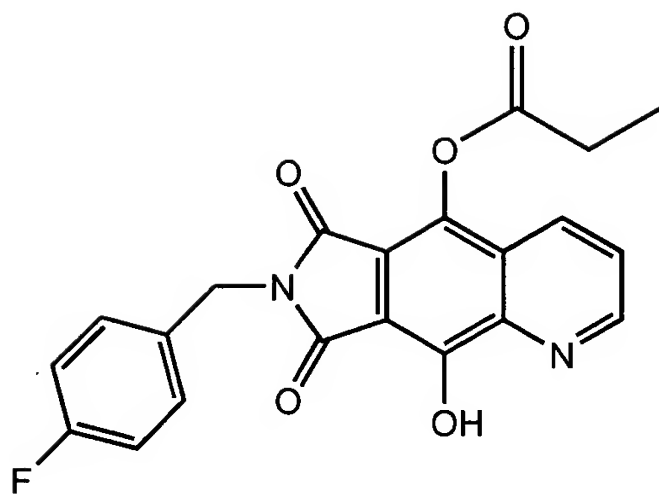
44. (previously presented): The compound of claim 36 wherein R^x is selected from the structures:



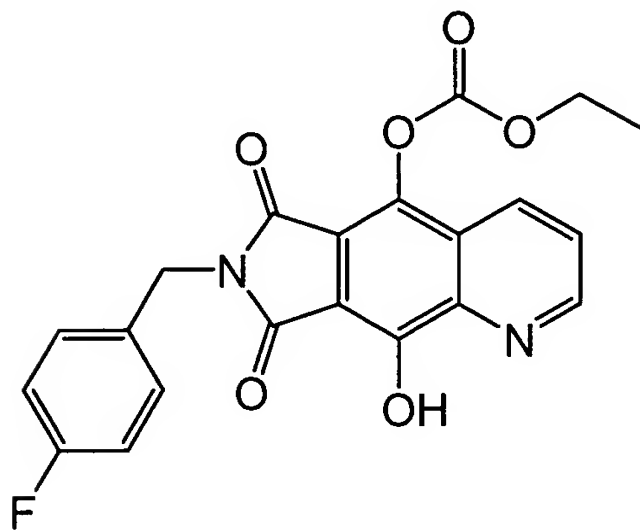
45. (once amended): A compound of [claim 9] selected from the structures:



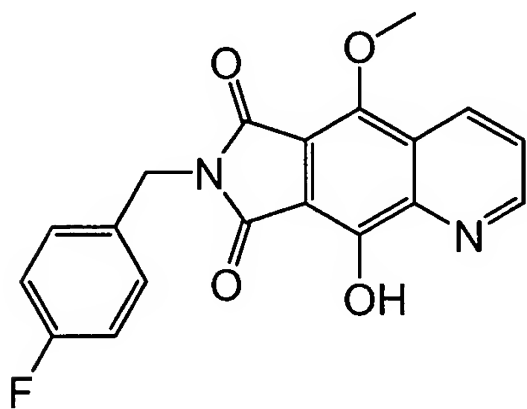
2



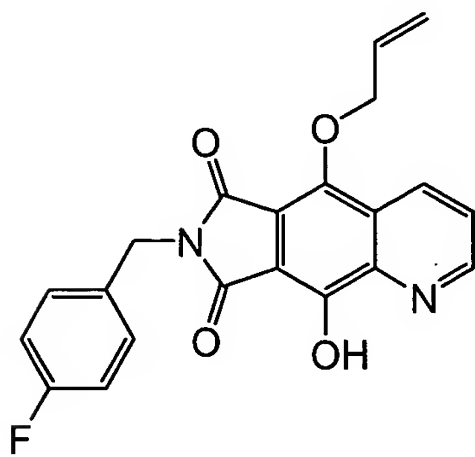
3



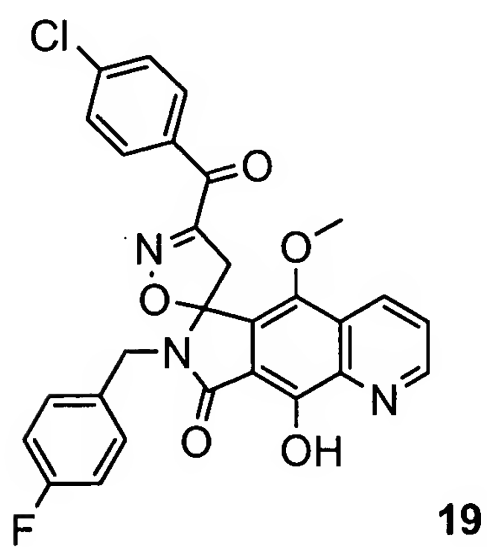
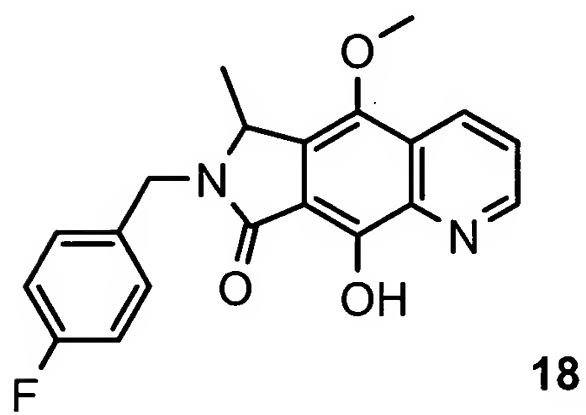
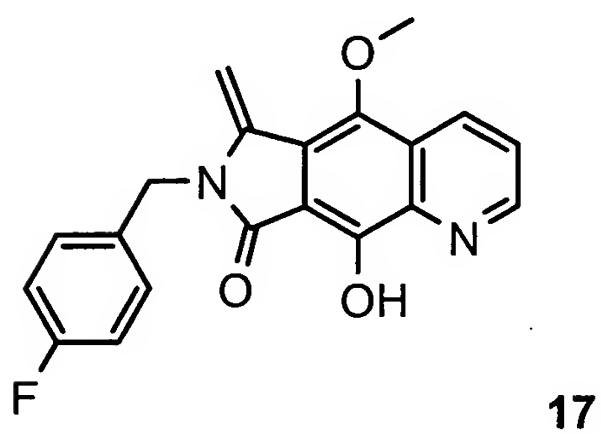
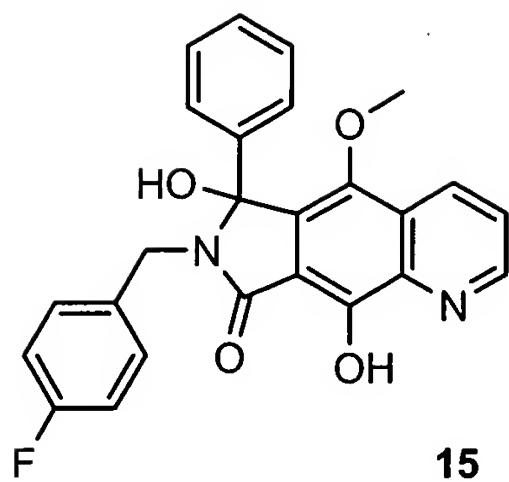
4

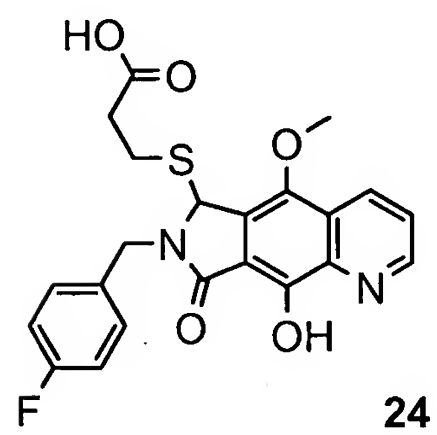
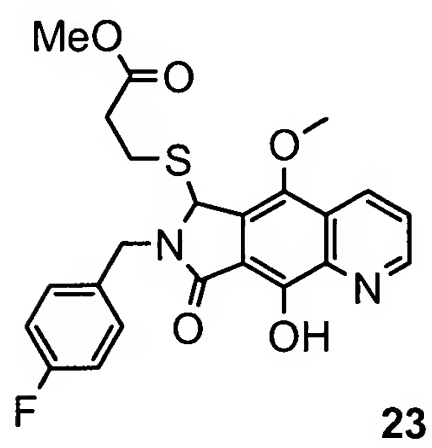
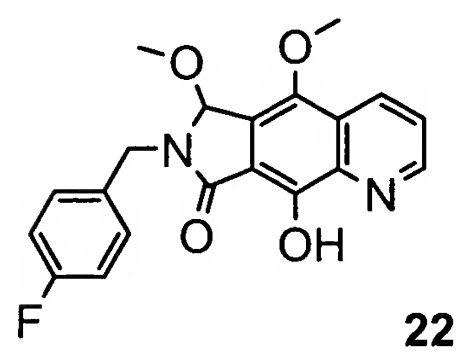
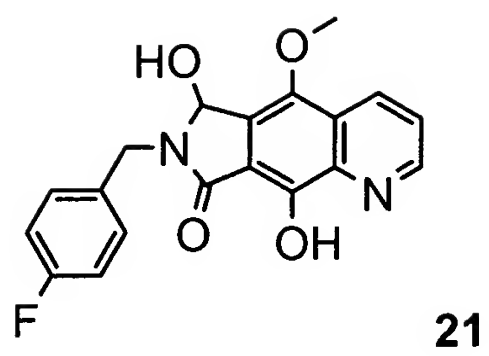


9

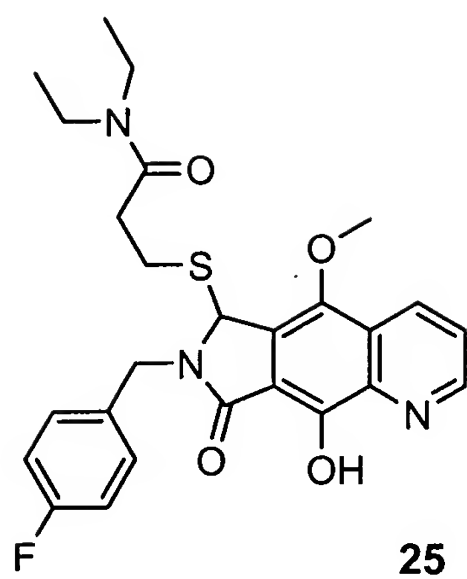


11

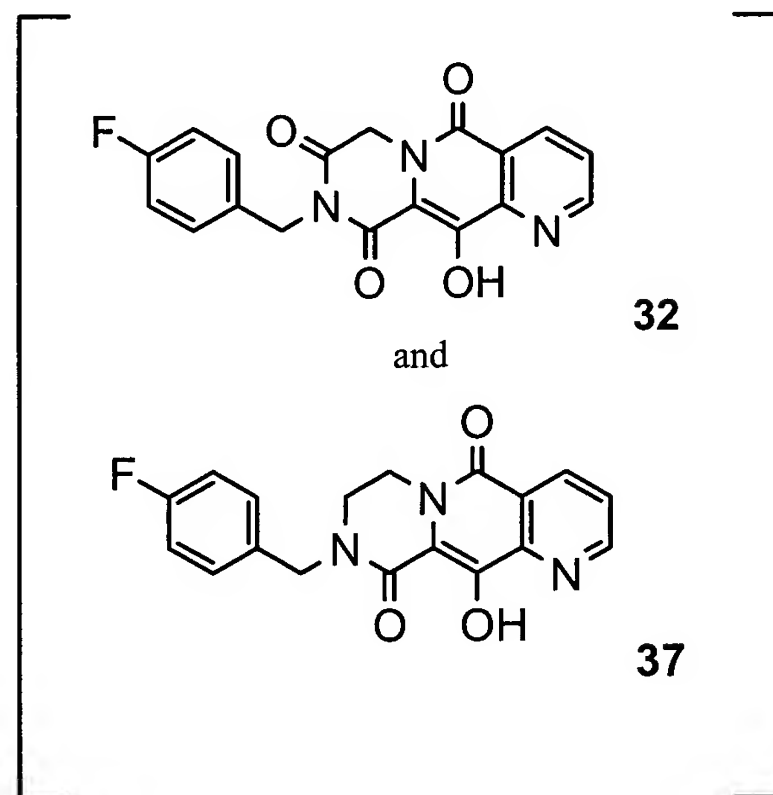




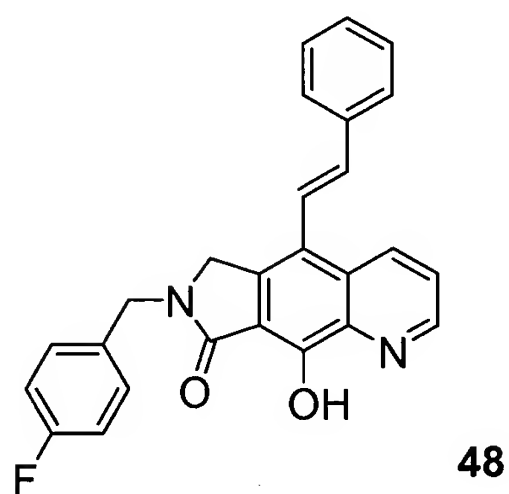
and

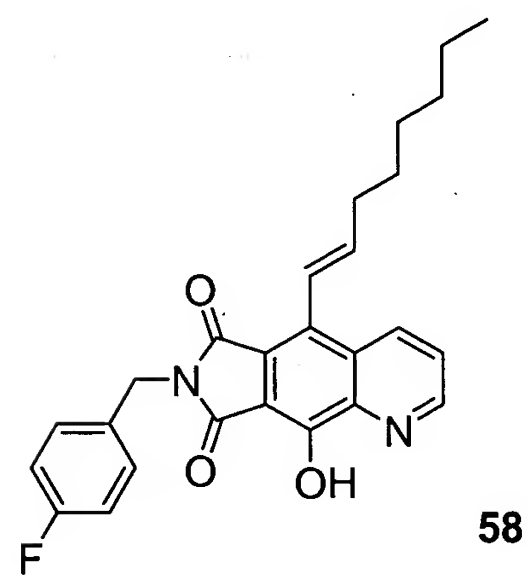
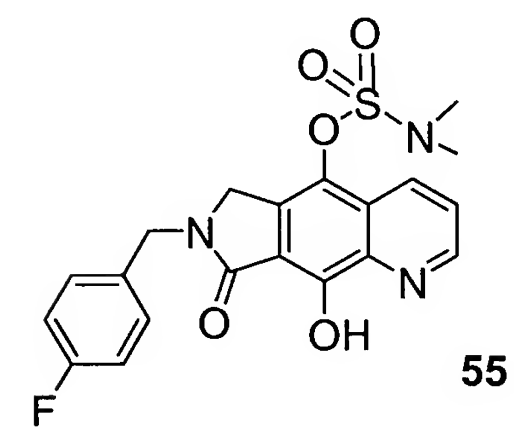
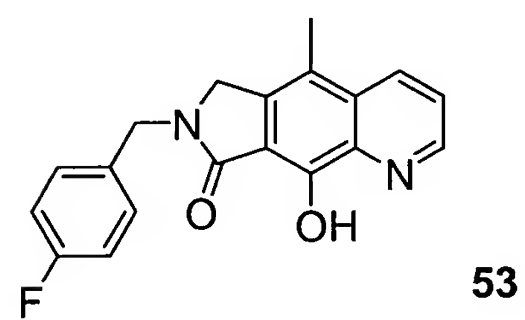
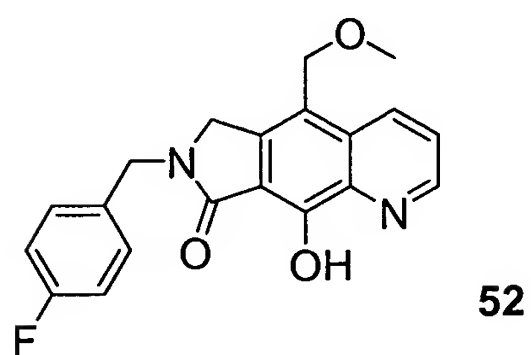
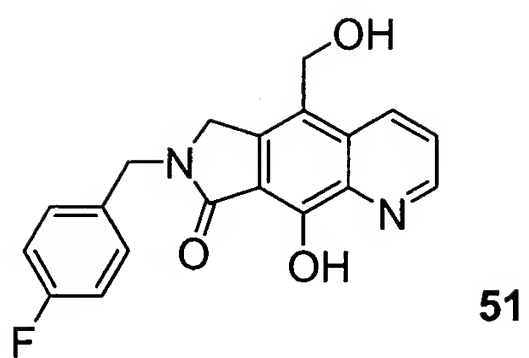


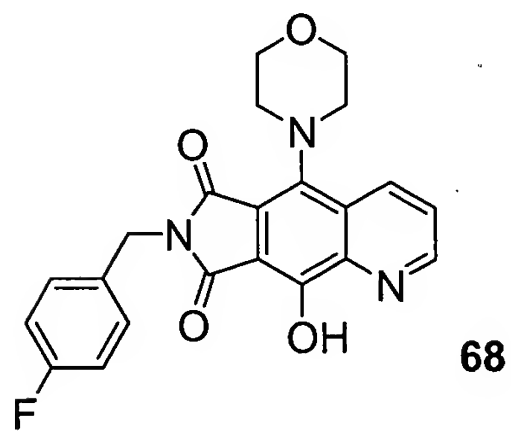
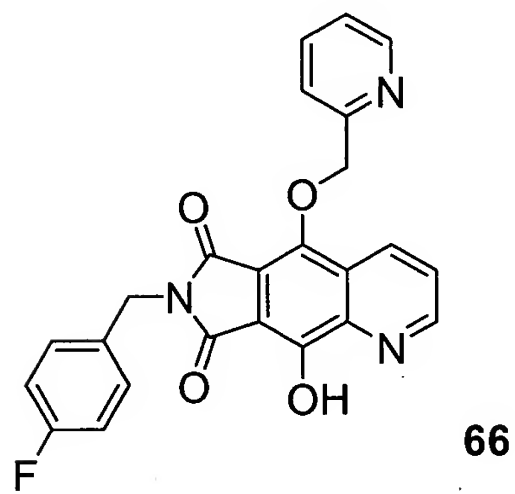
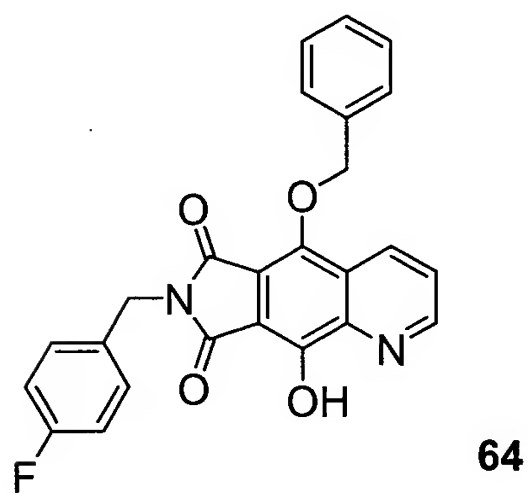
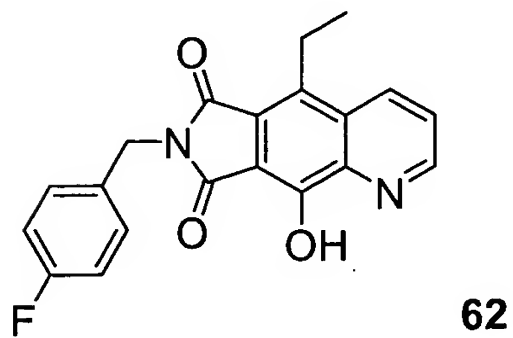
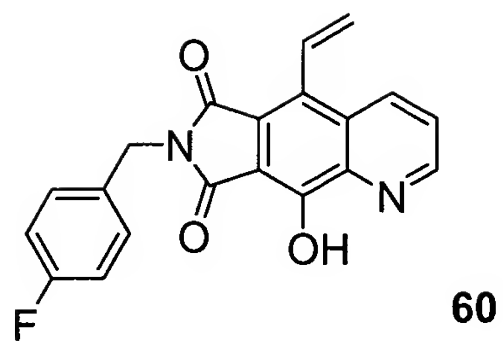
46. (once amended): A compound of claim 1 [11 selected from the structures:]
wherein none of R^2 , R^3 , R^4 , R , or R^{x2} is a prodrug moiety

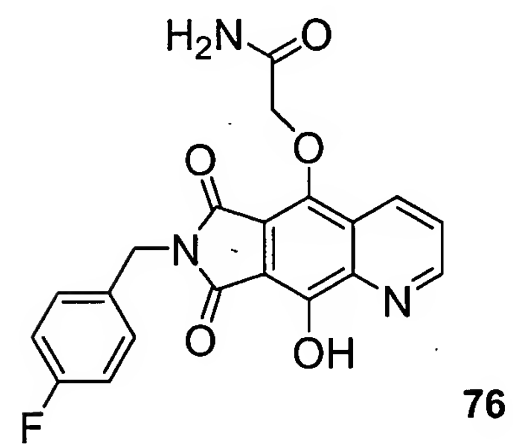
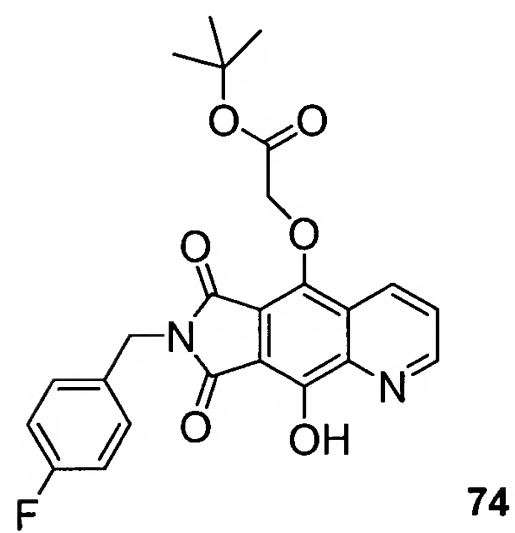
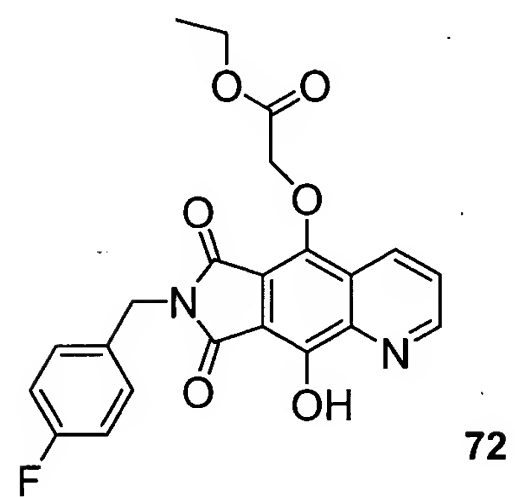
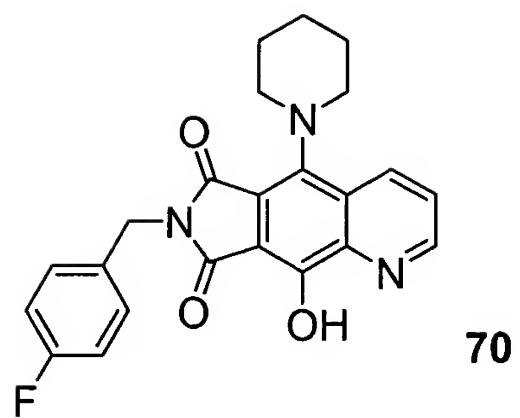


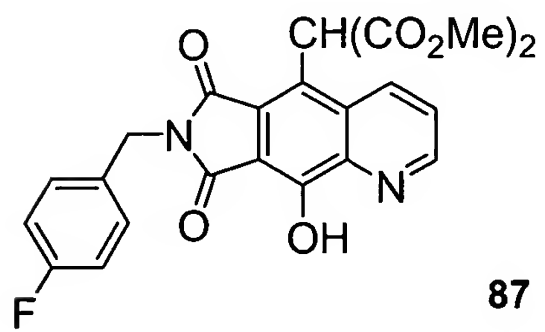
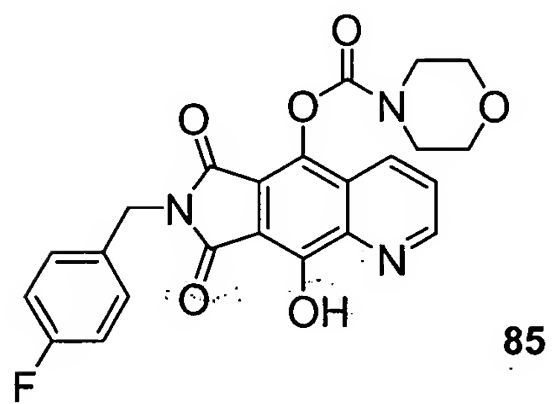
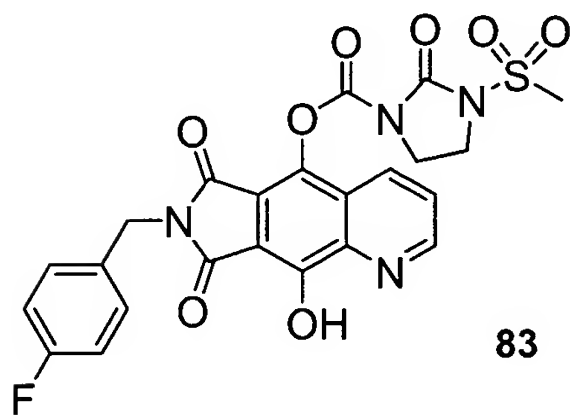
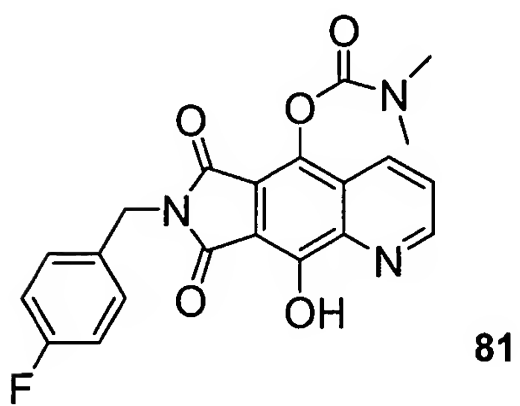
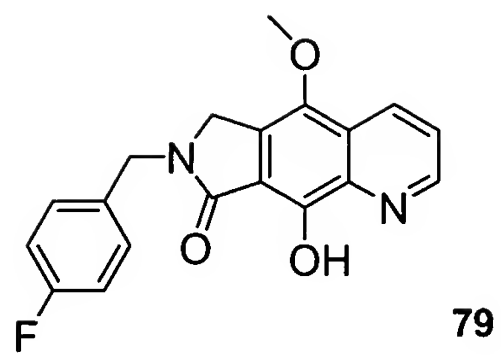
47. (once amended): A compound of [claim 9] selected from the structures:

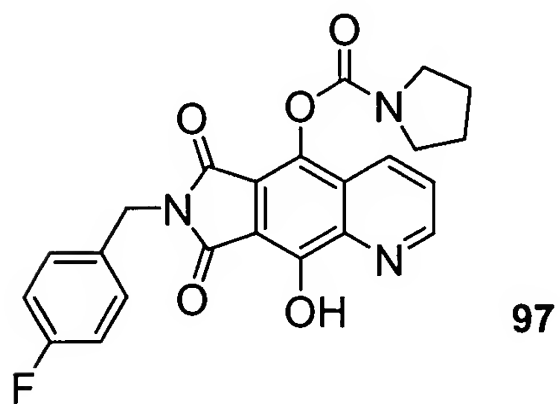
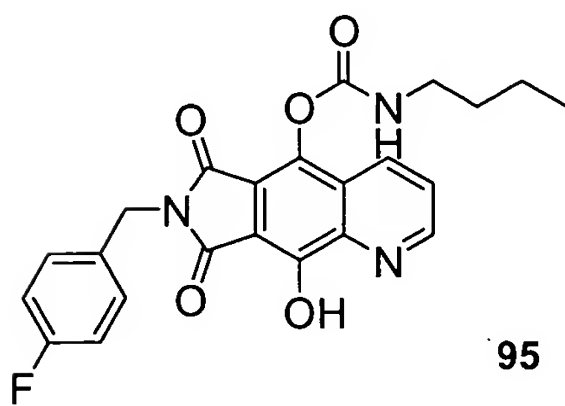
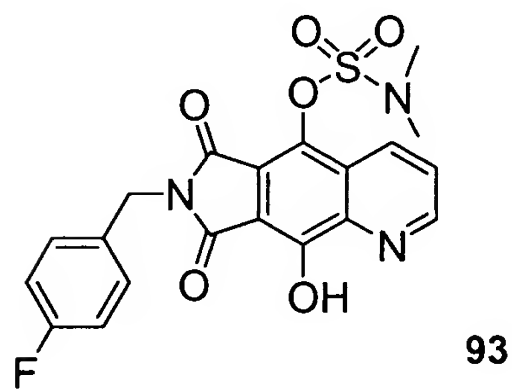
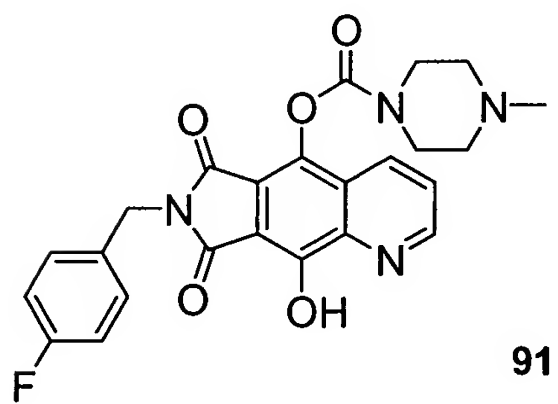
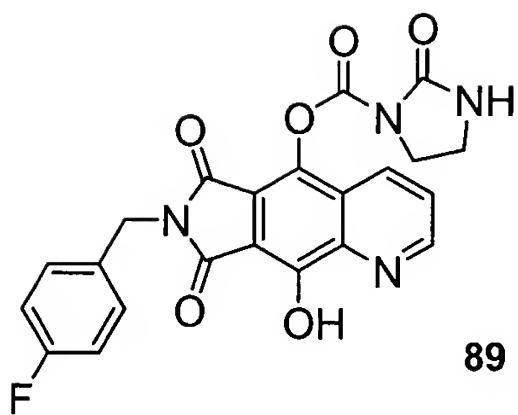


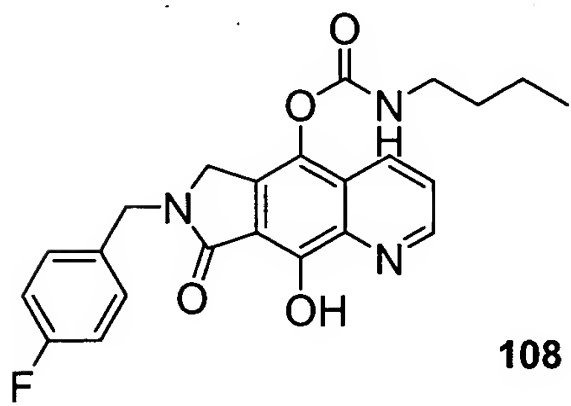
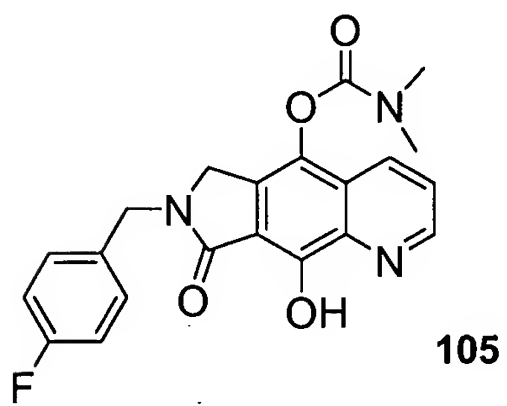
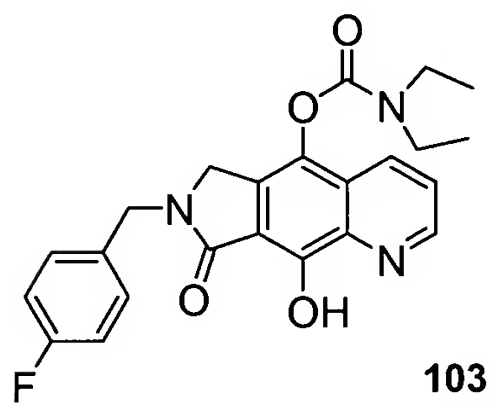
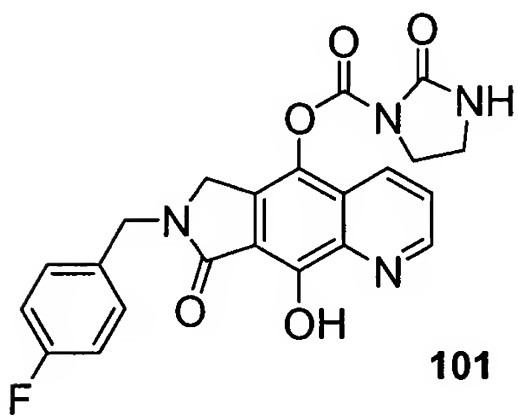
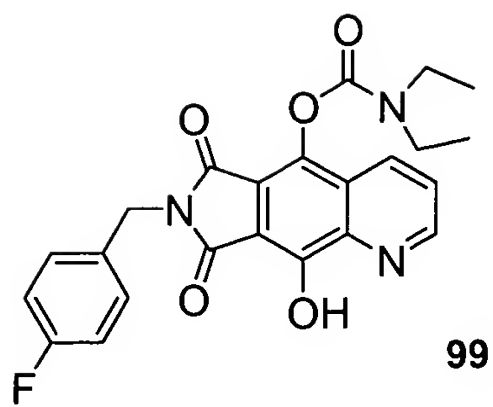


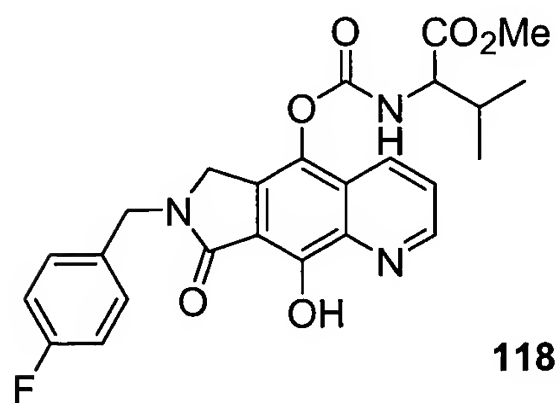
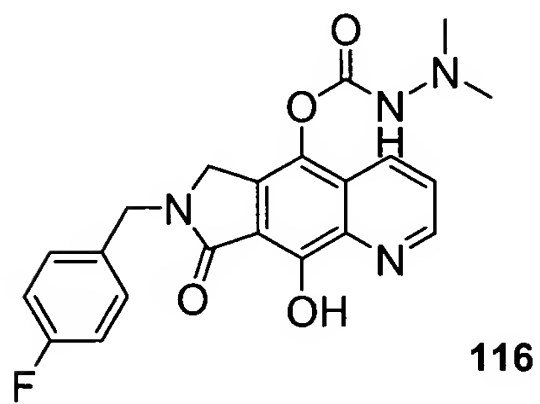
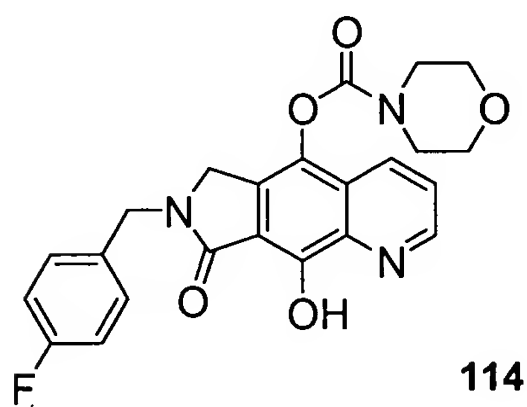
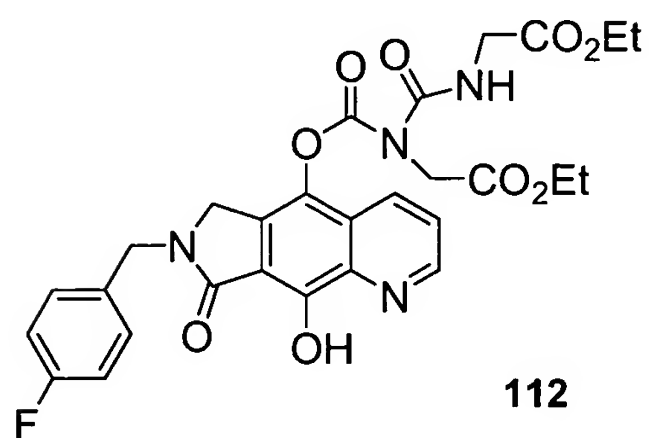
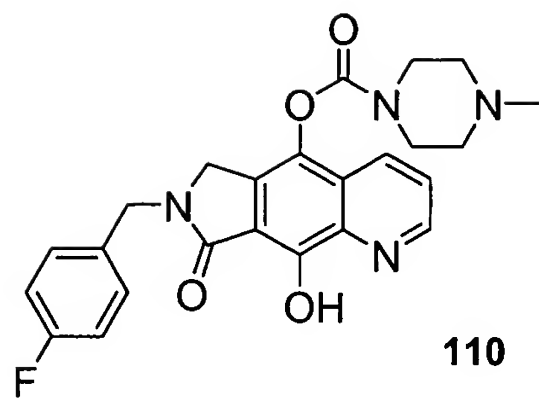


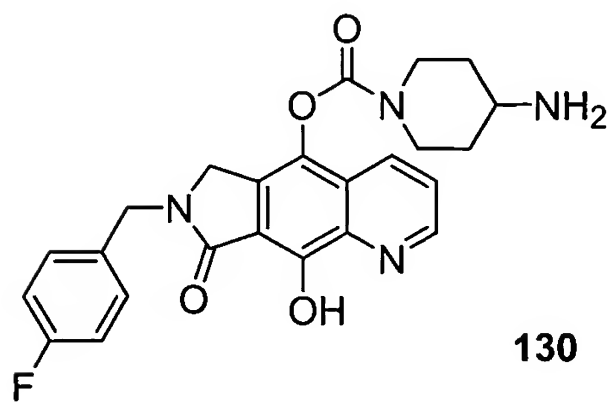
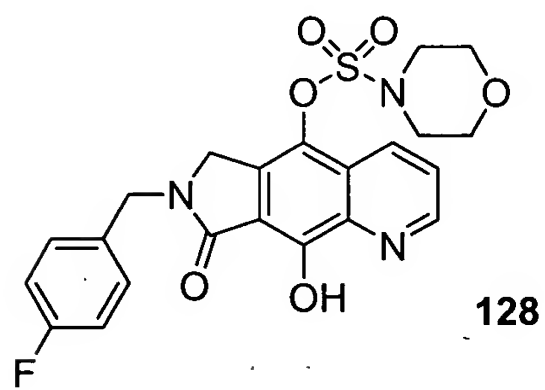
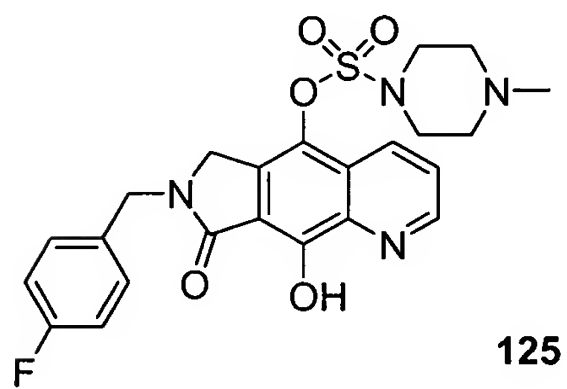
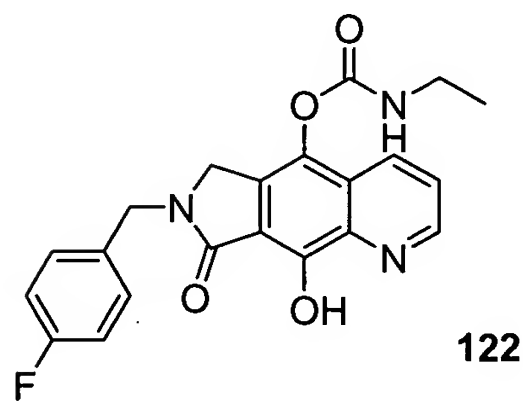
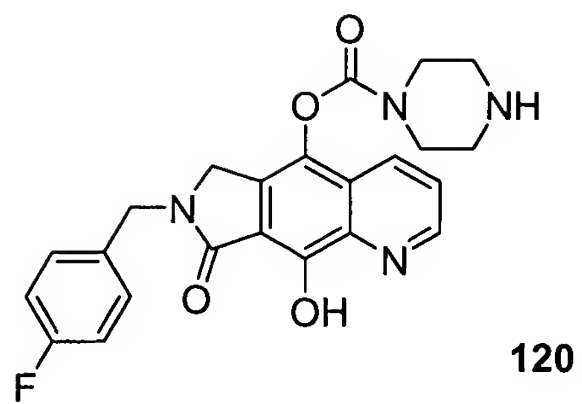


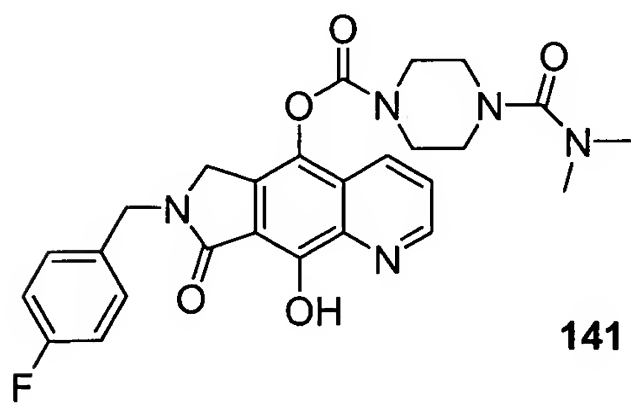
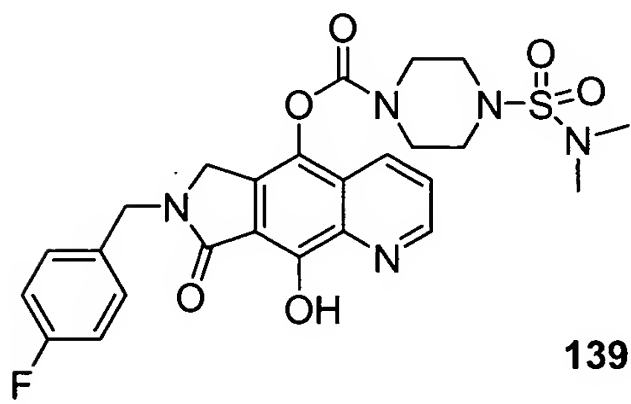
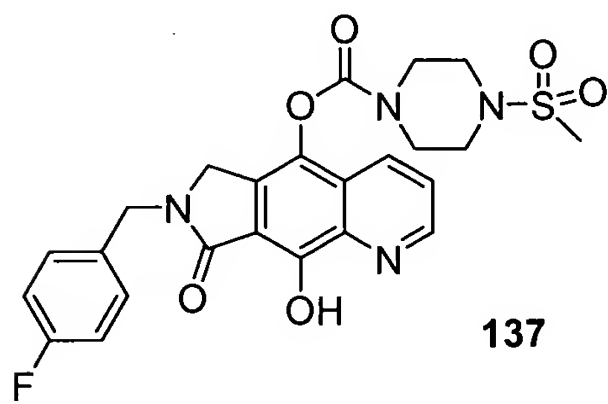
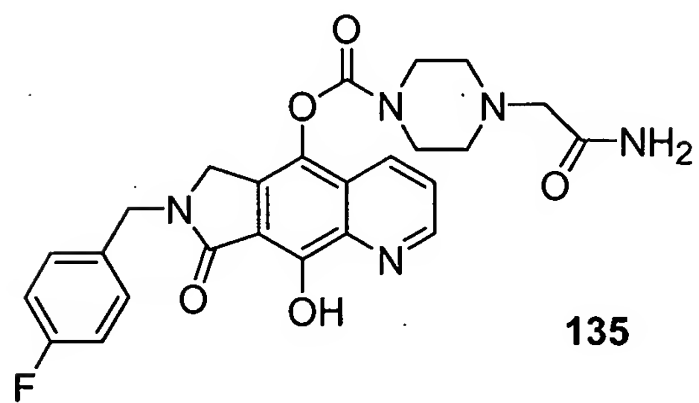
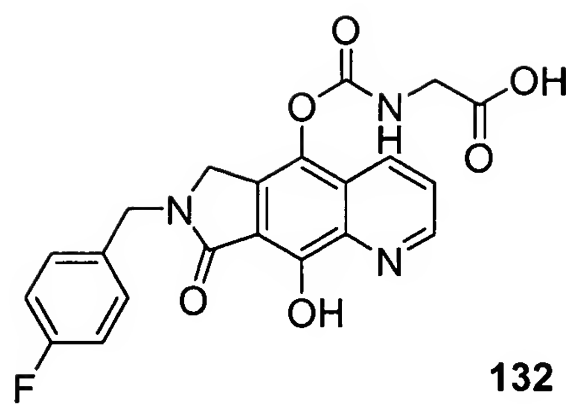


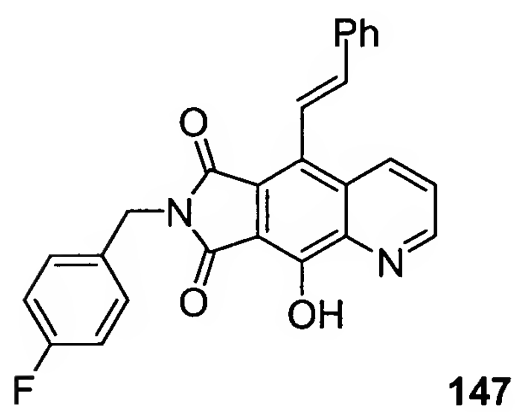
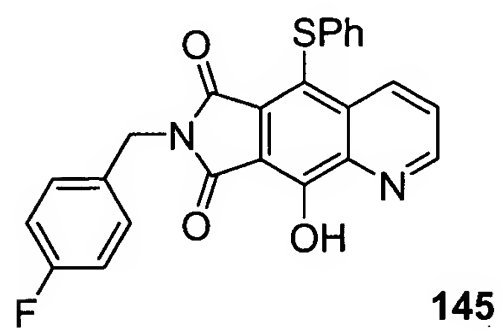
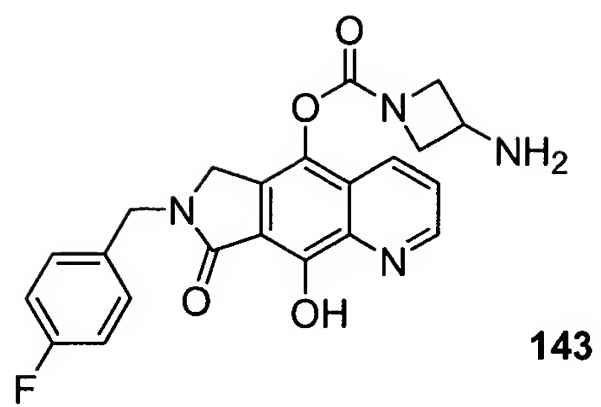


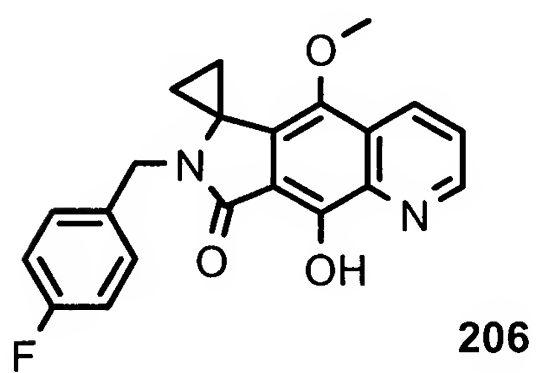
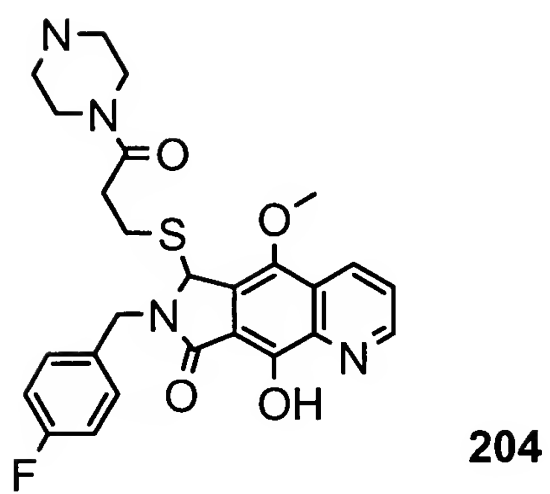
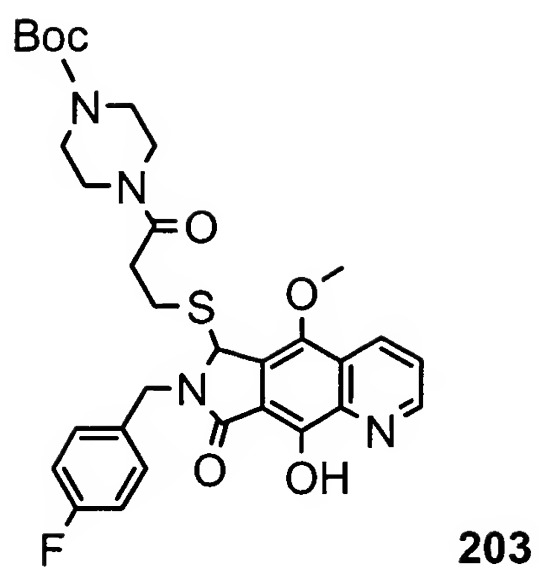


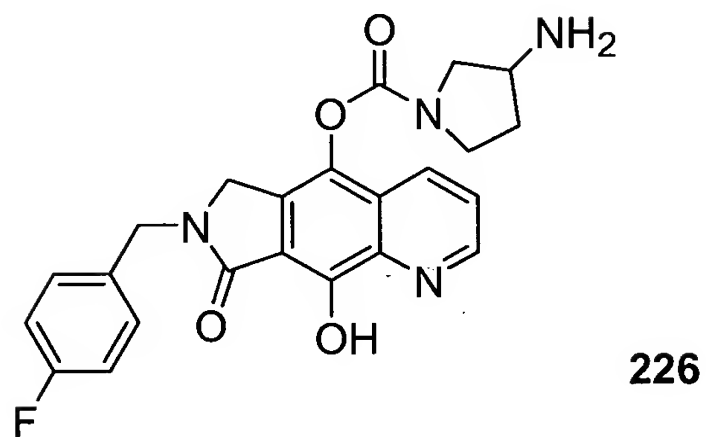
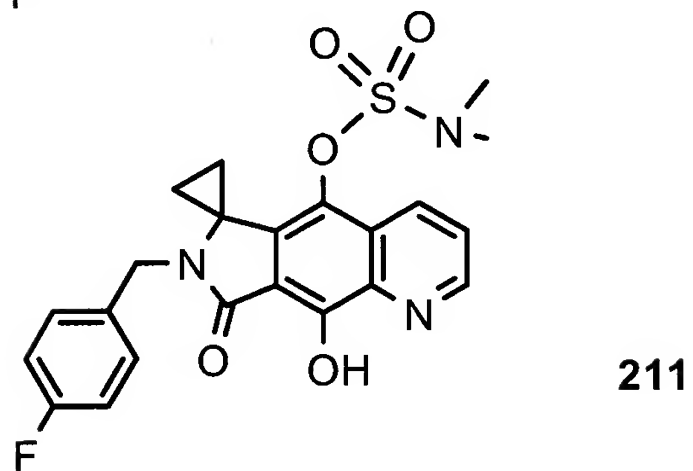
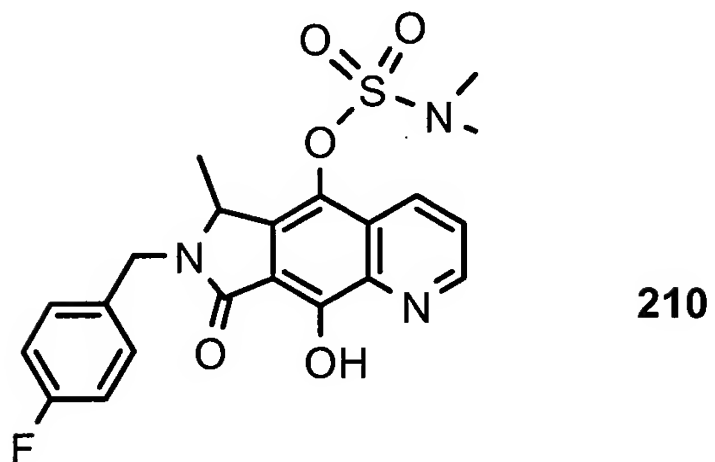
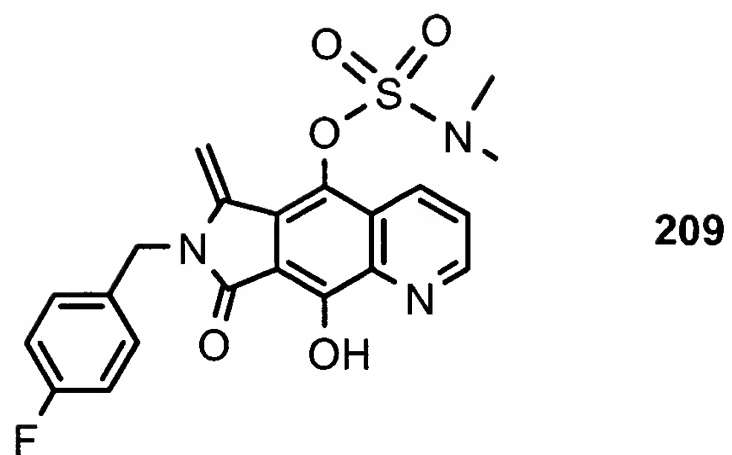


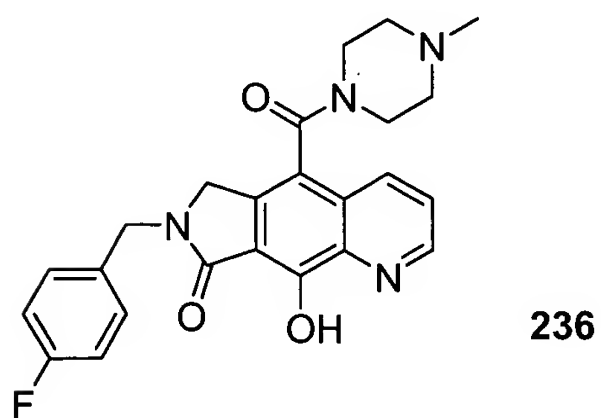
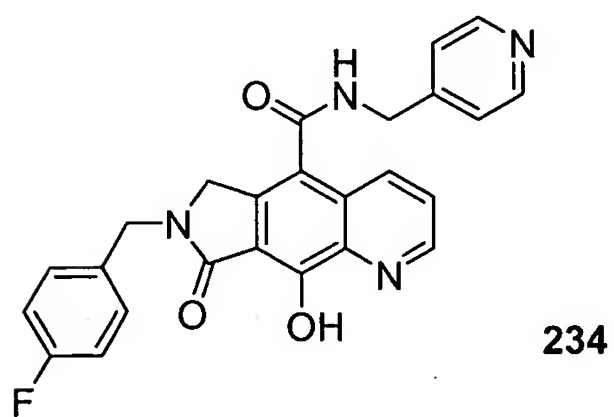
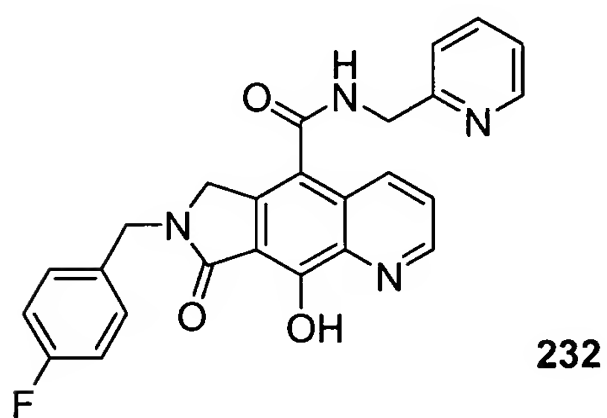
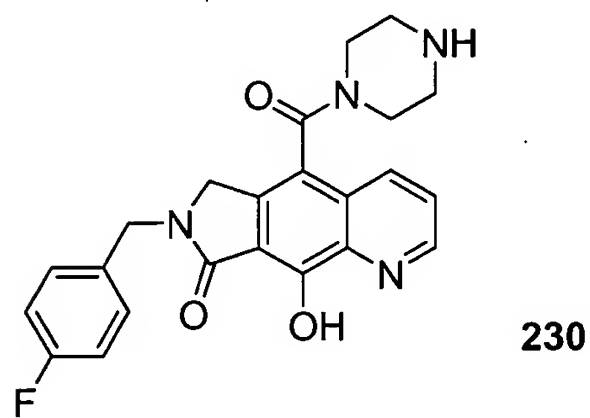
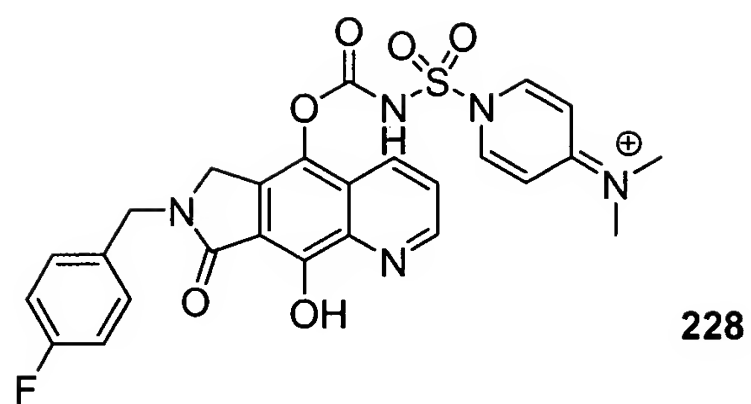


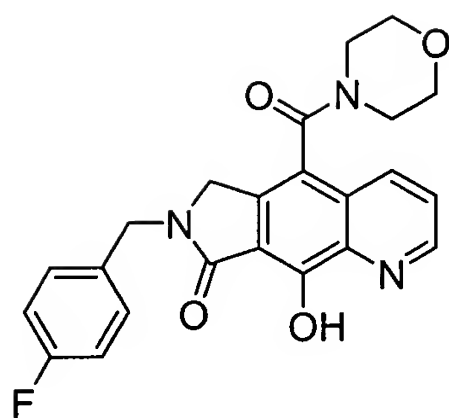




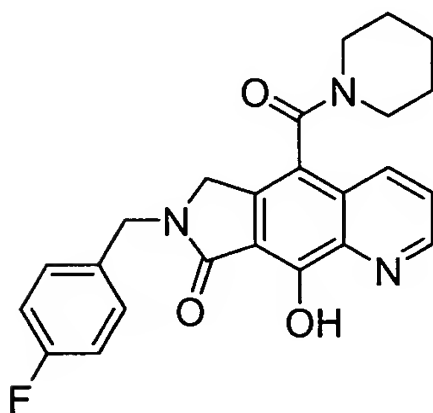




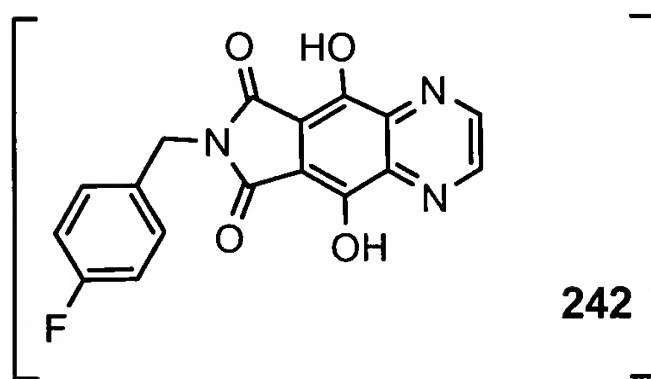




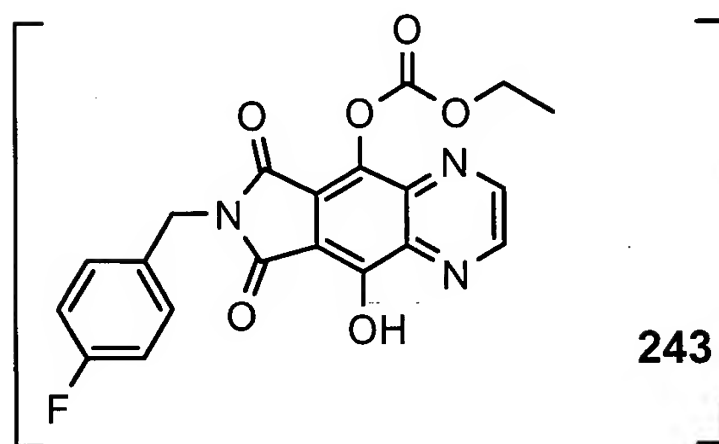
238



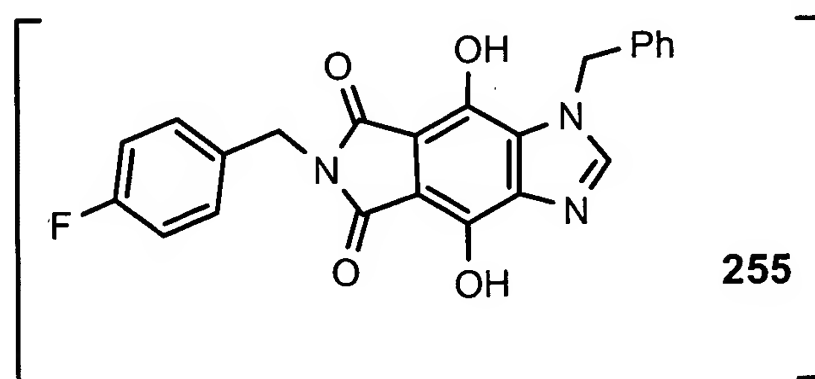
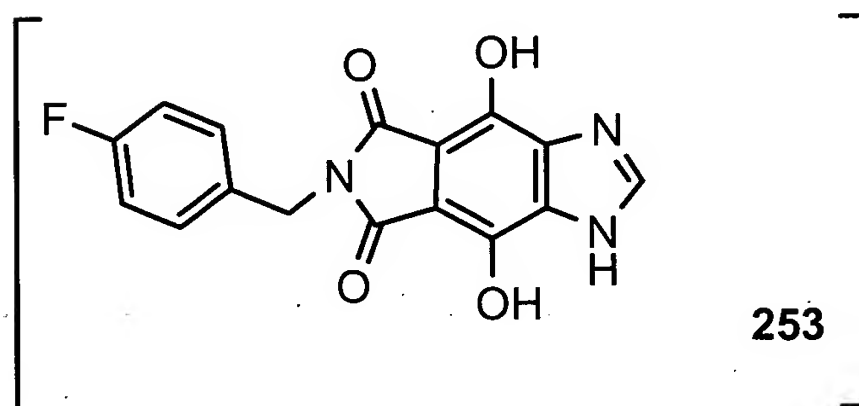
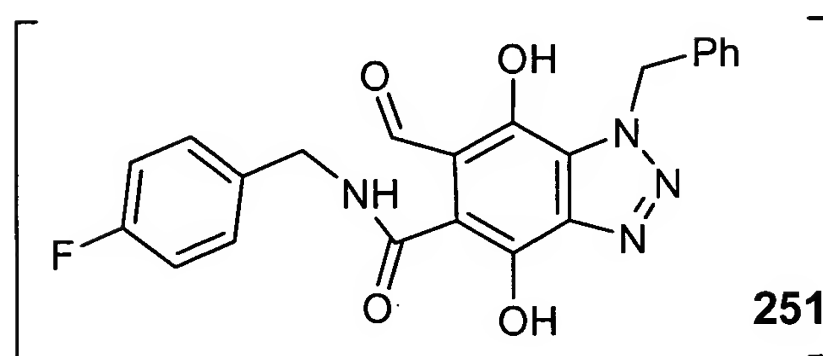
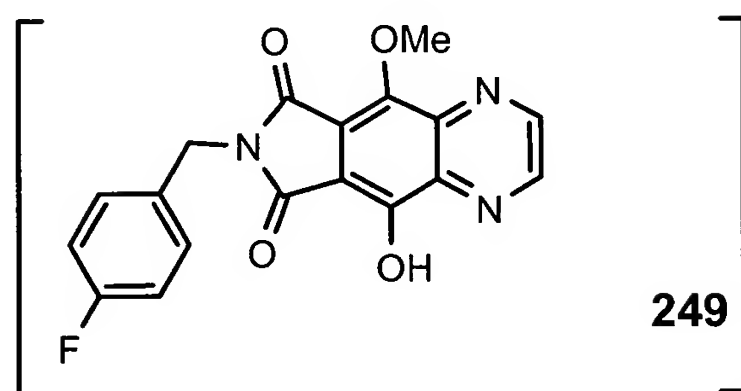
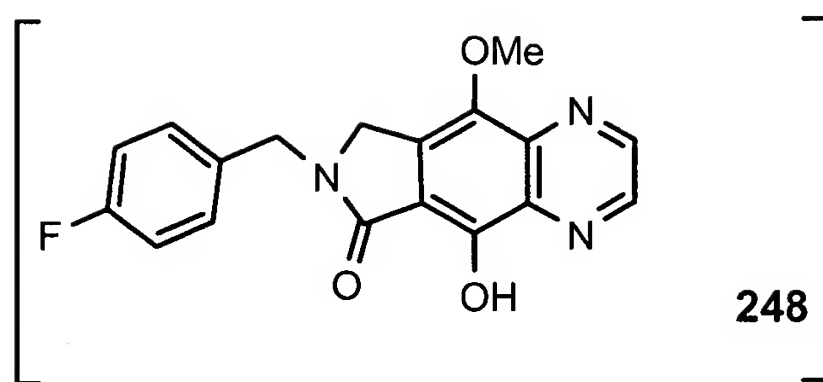
240

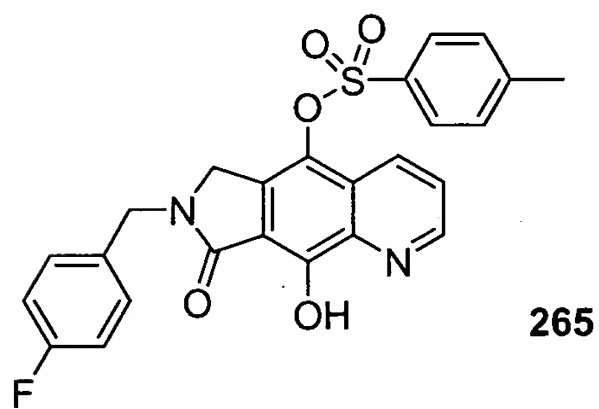
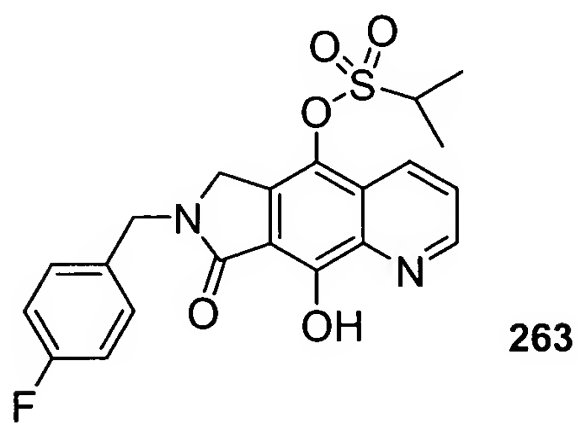
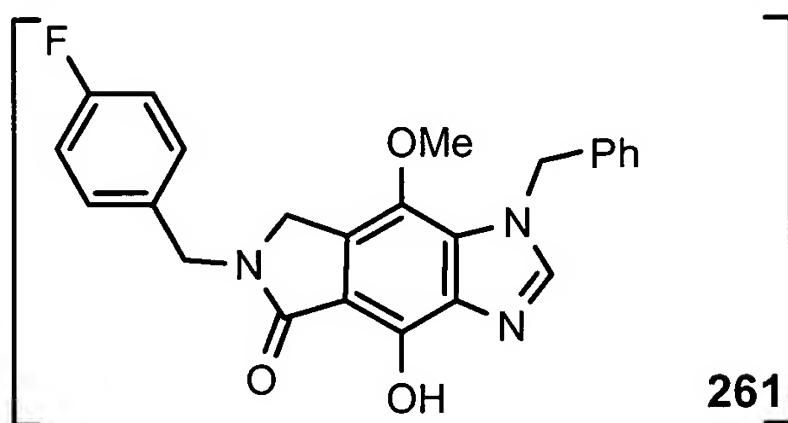
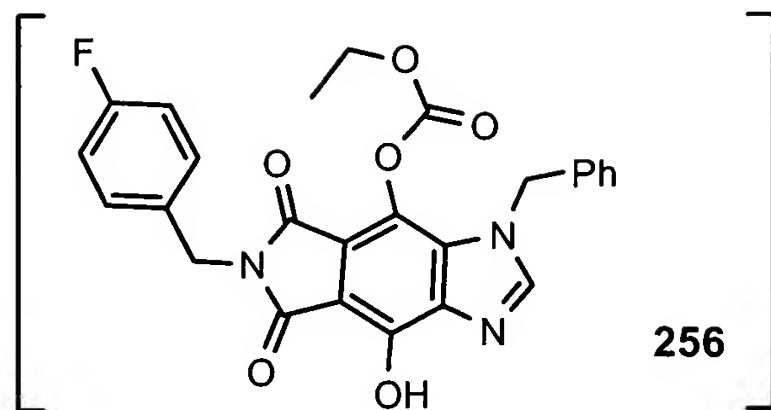


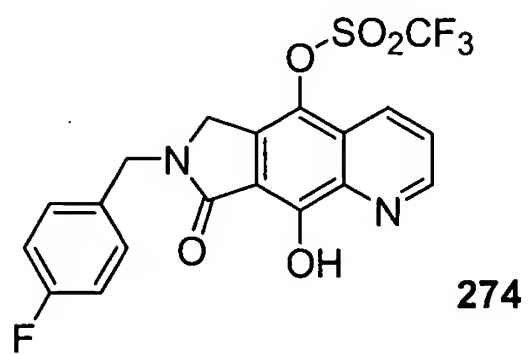
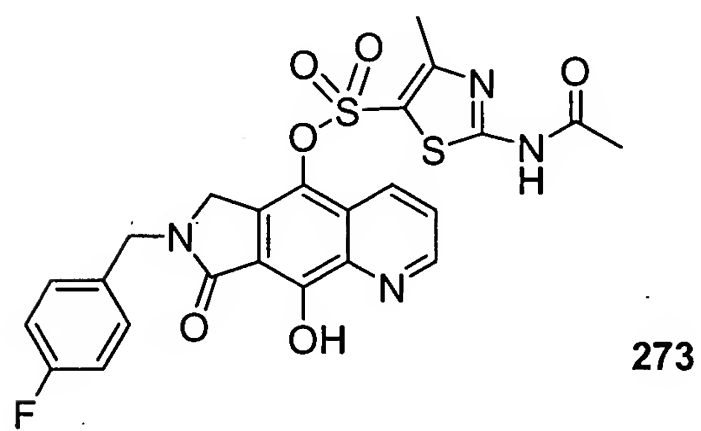
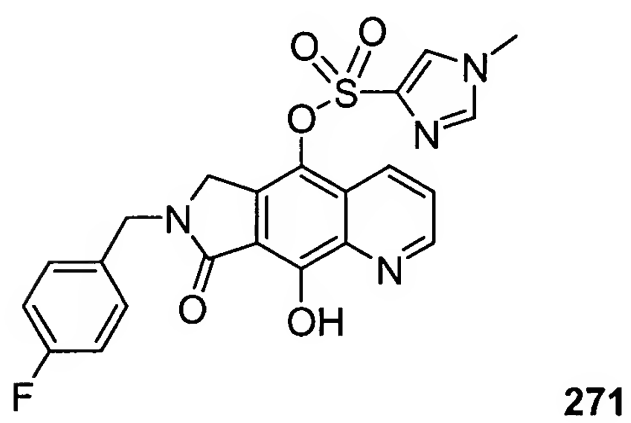
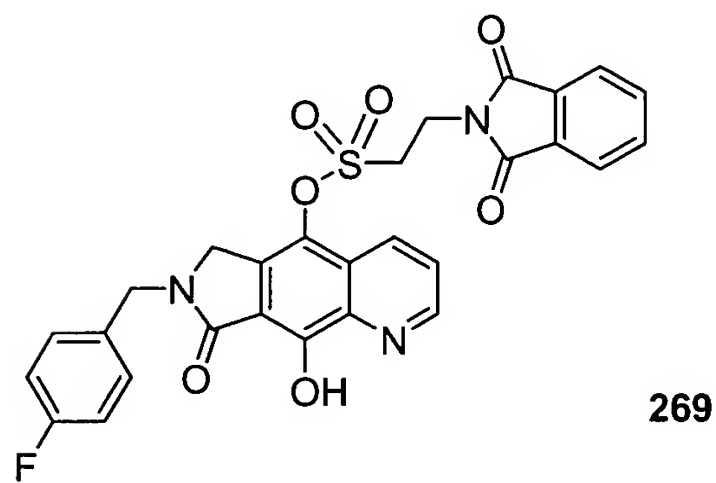
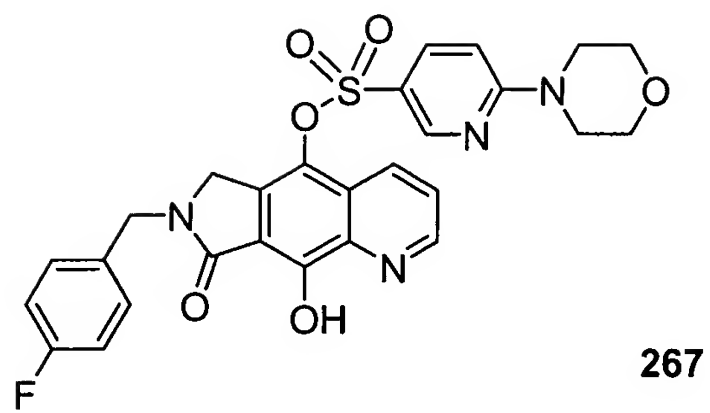
242

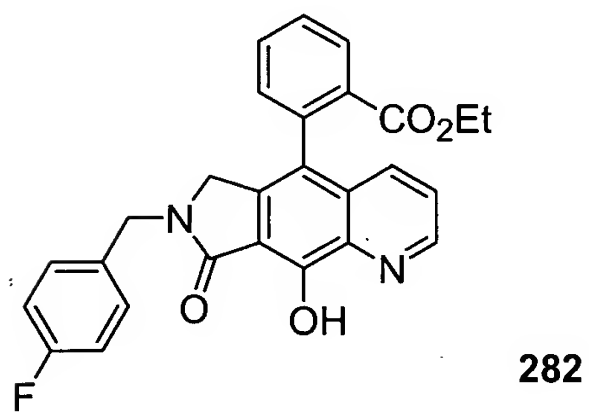
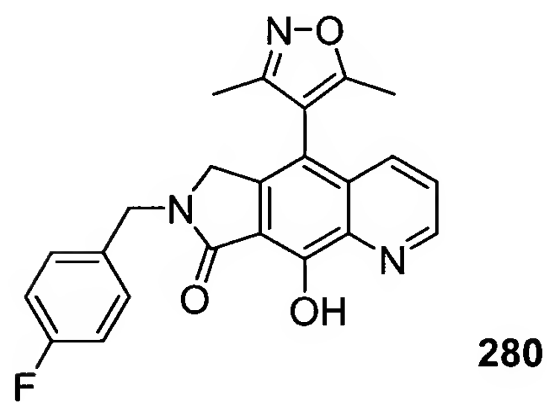
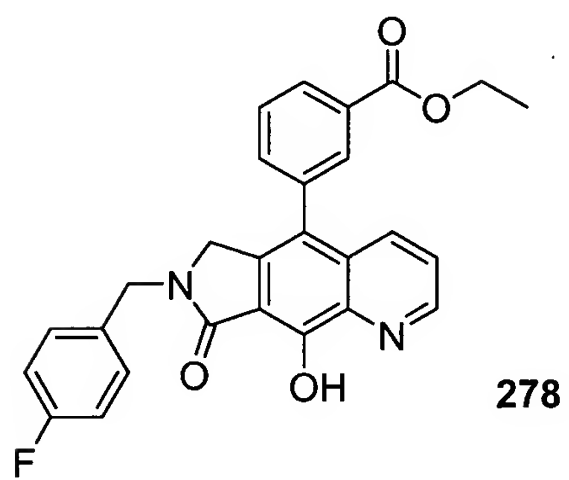
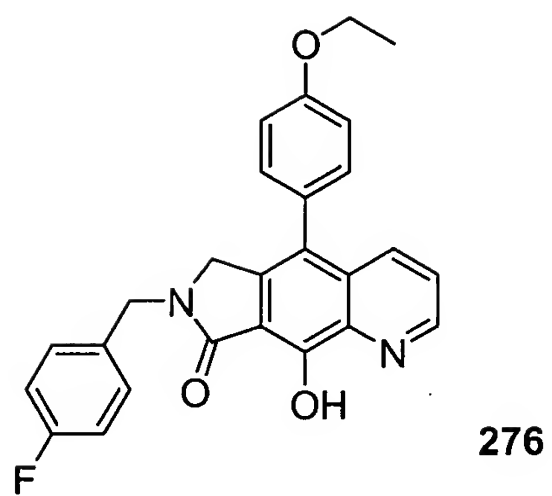


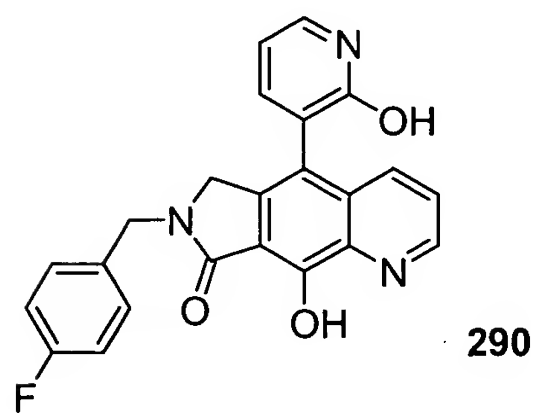
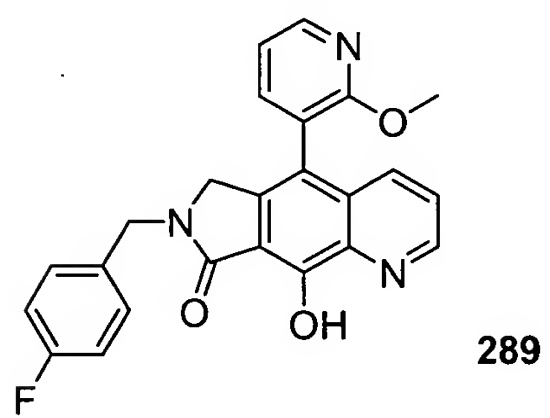
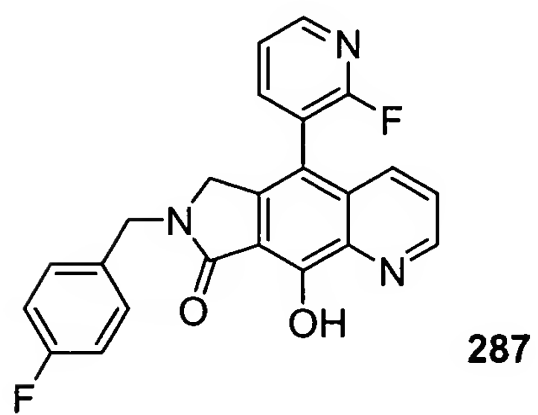
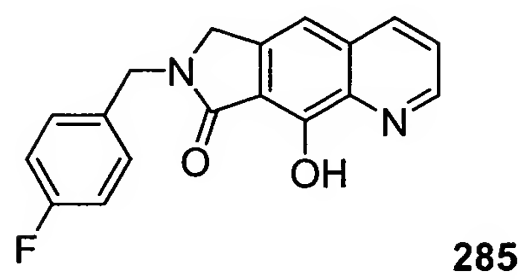
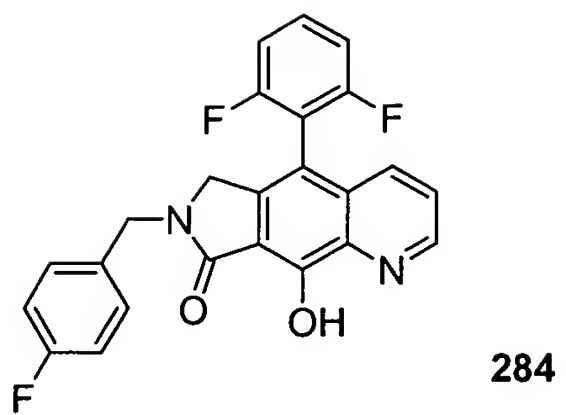
243

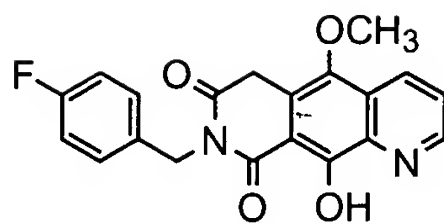




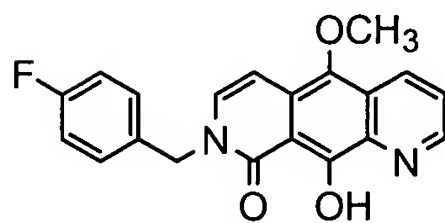




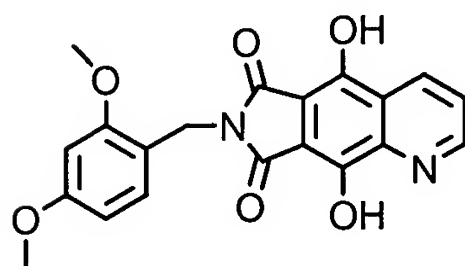




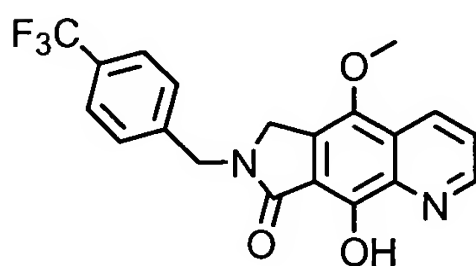
296



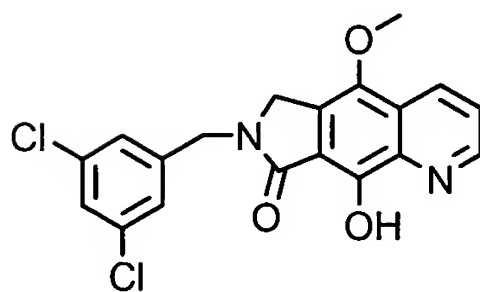
298



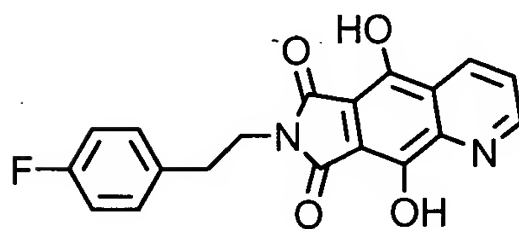
300



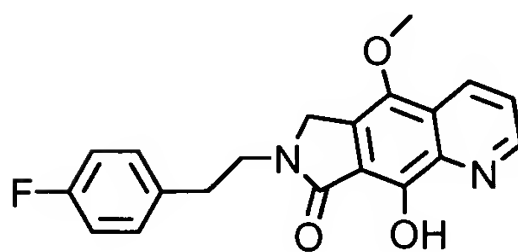
306



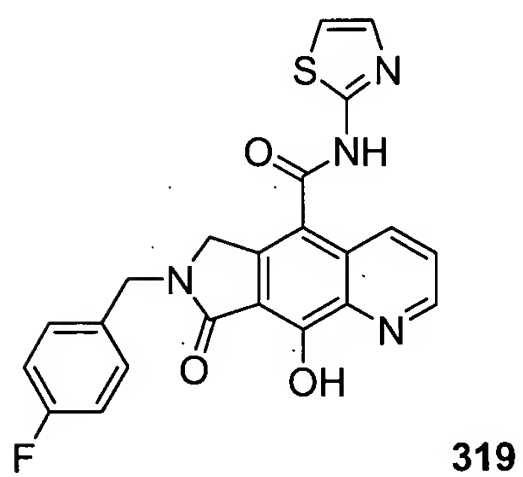
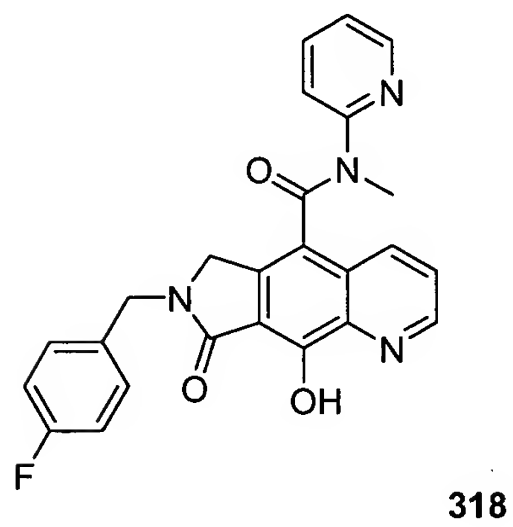
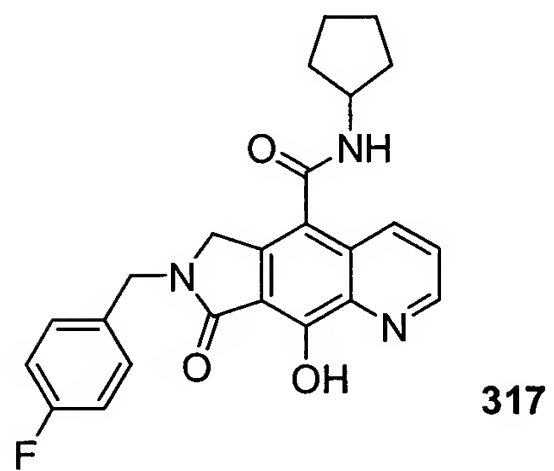
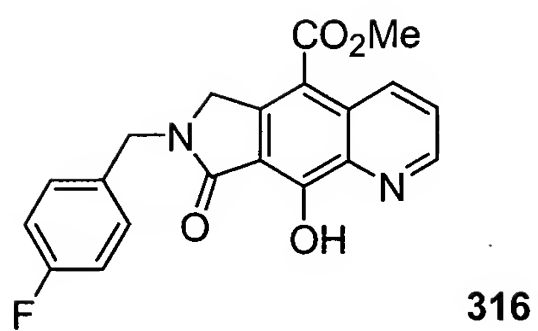
308

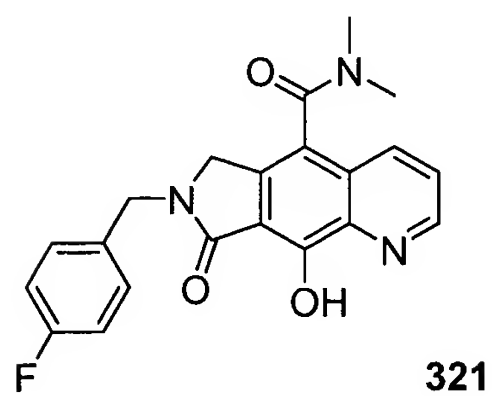
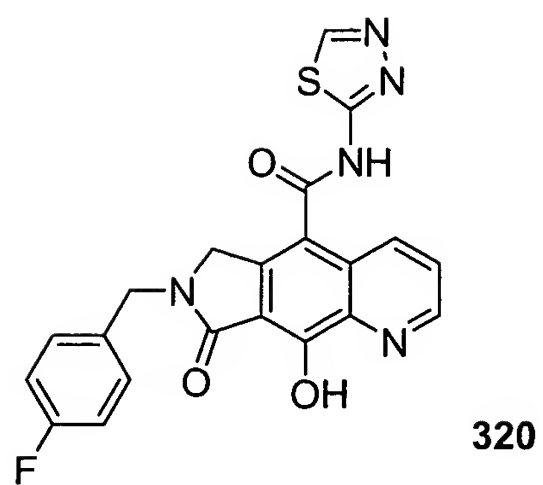


310

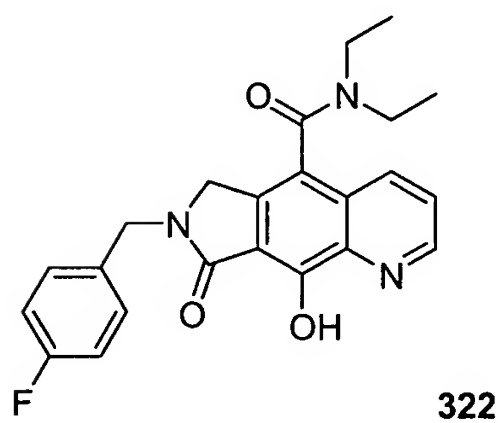


313

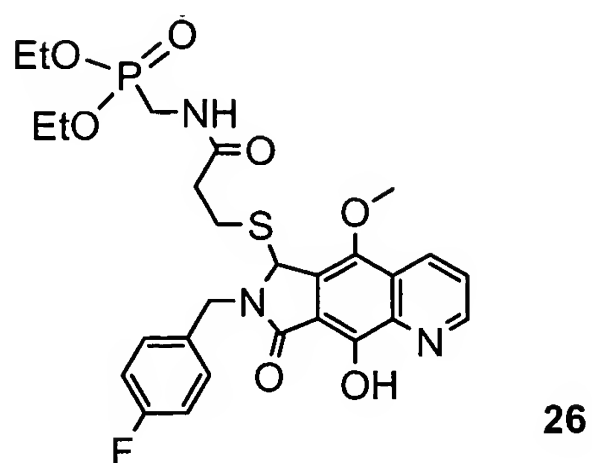


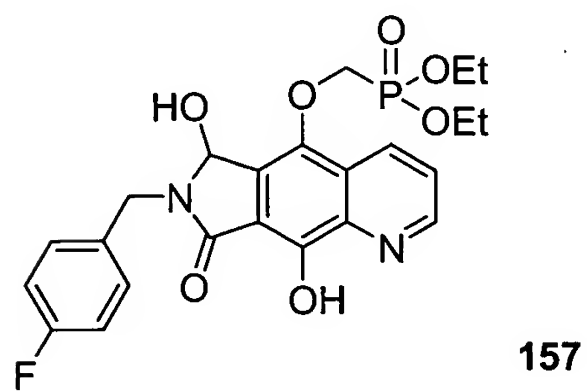
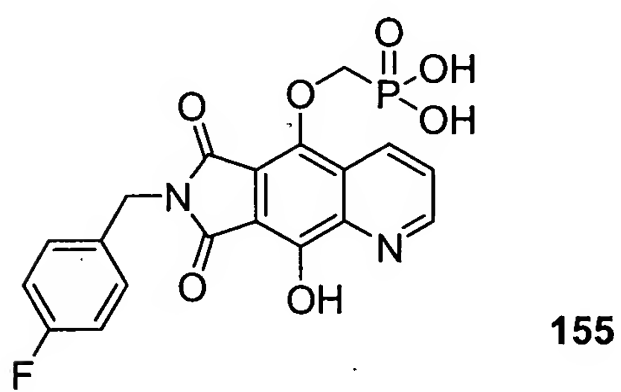
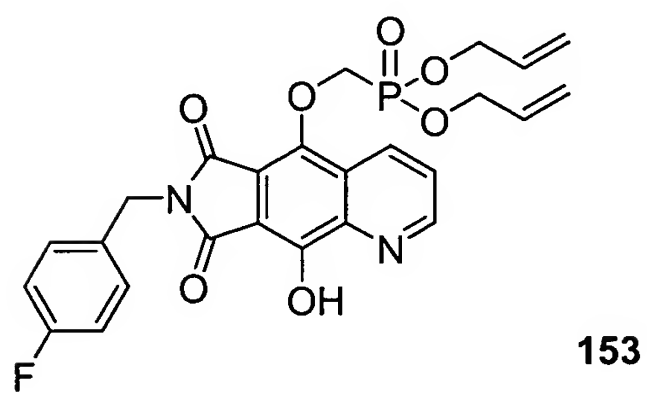
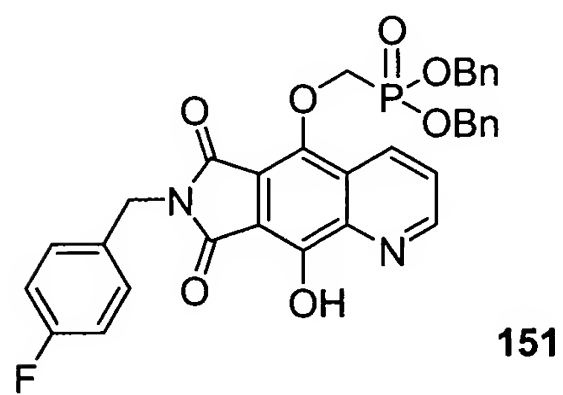
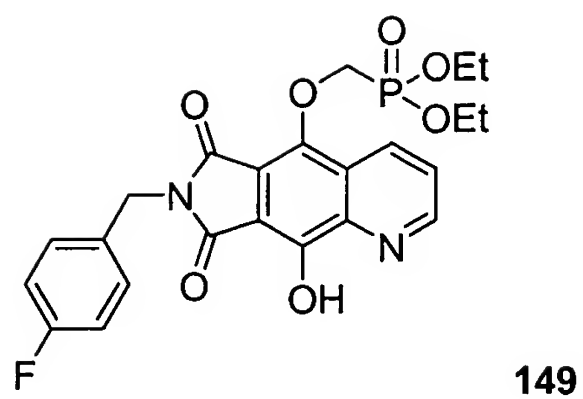


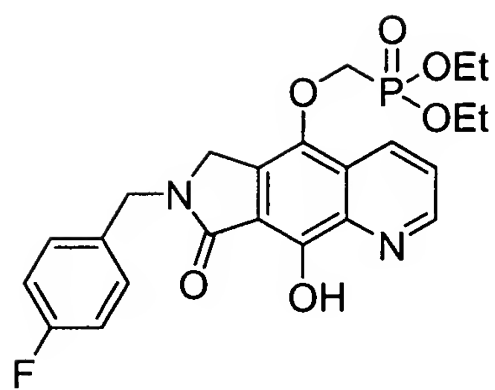
and



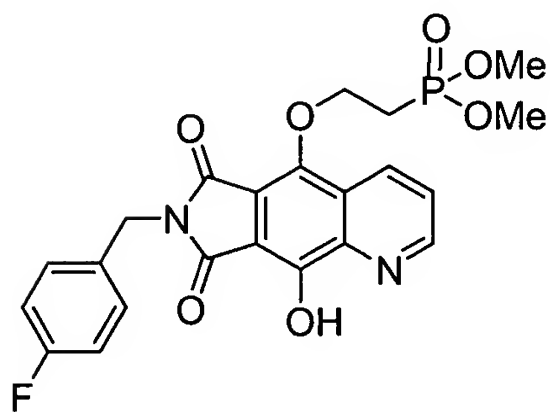
48. (once amended): A compound [of claim 13] selected from the structures:



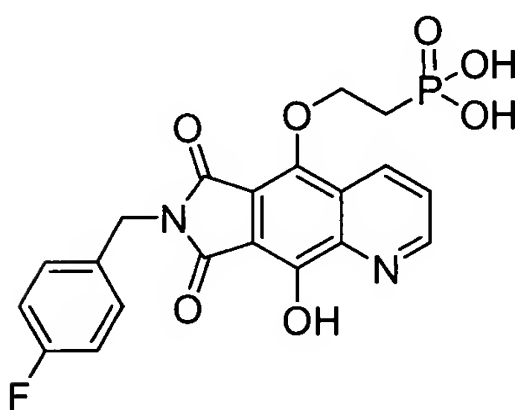




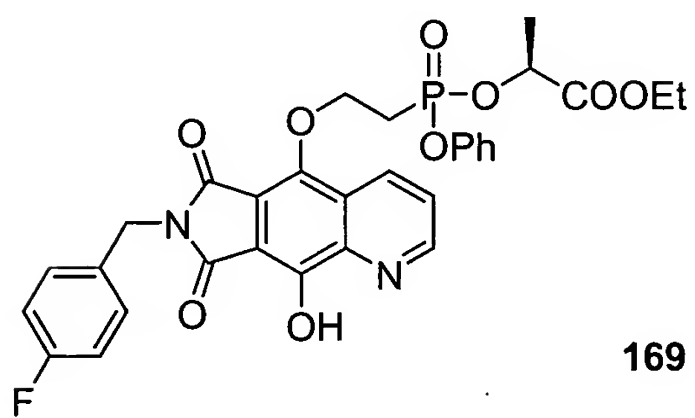
158



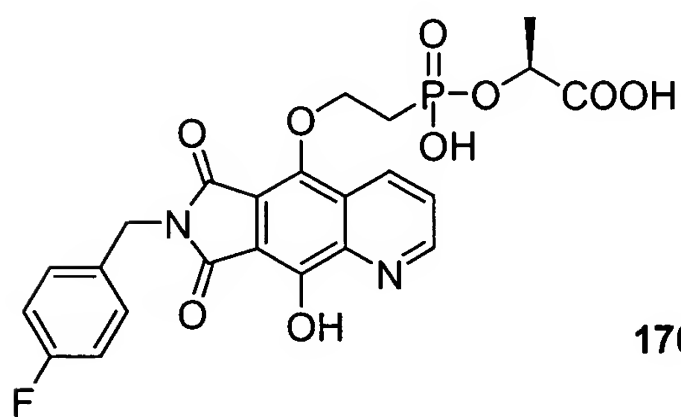
160



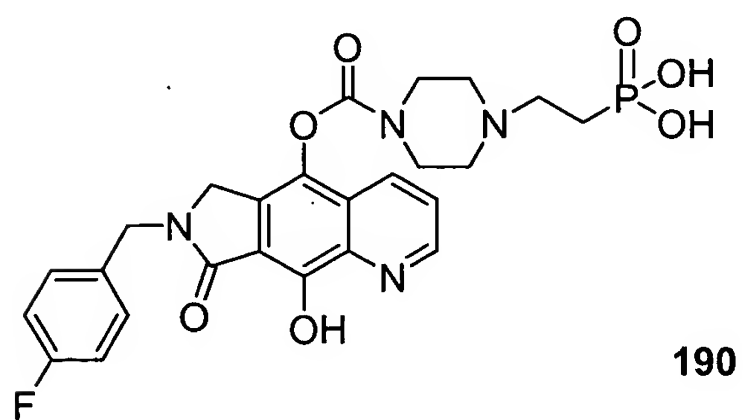
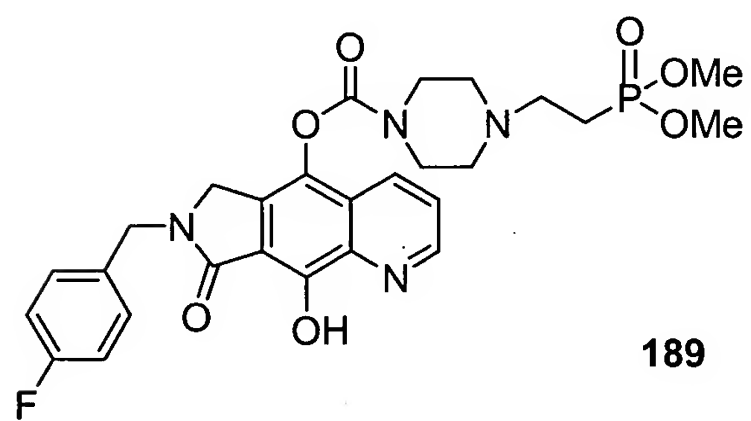
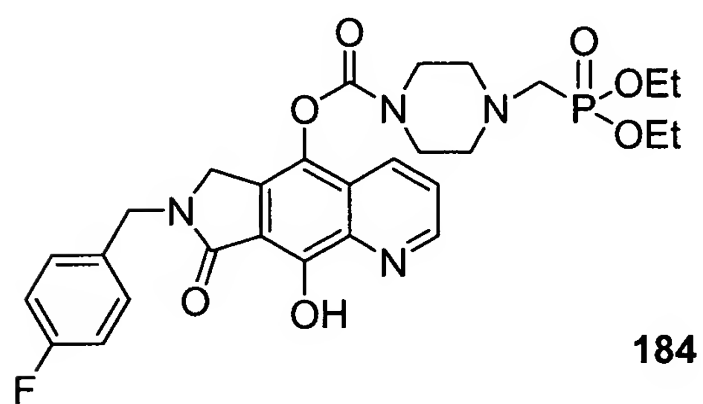
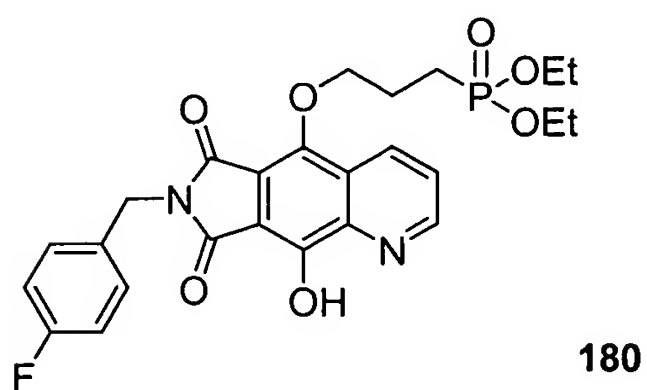
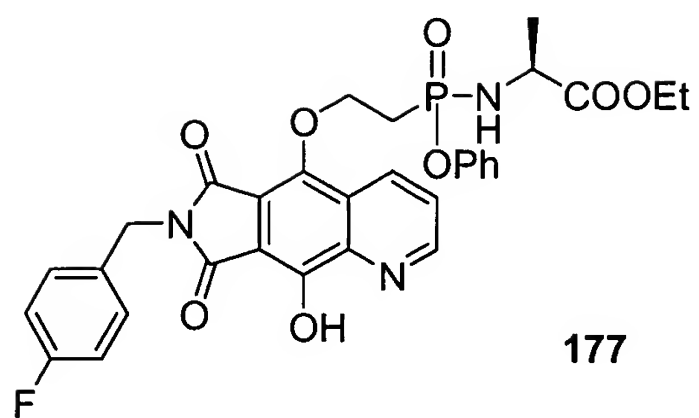
165

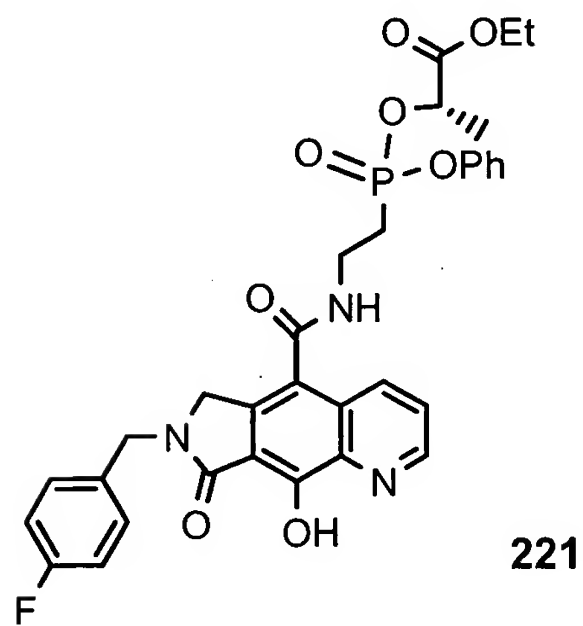
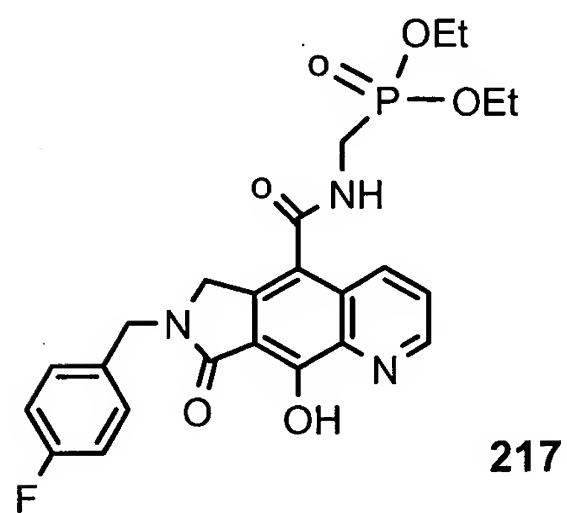
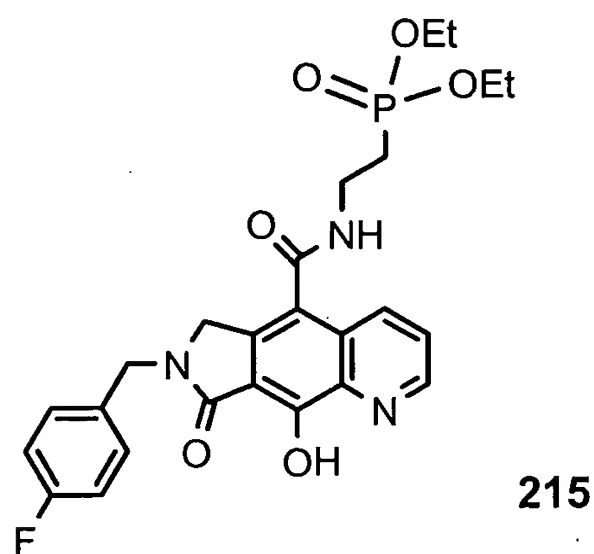
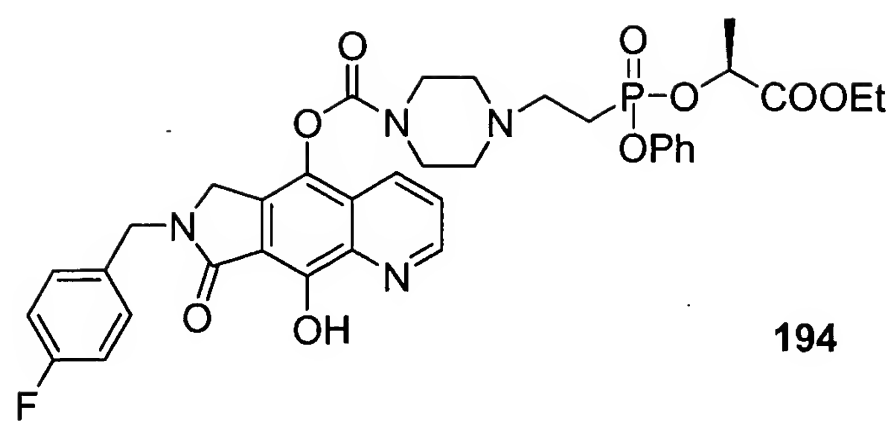


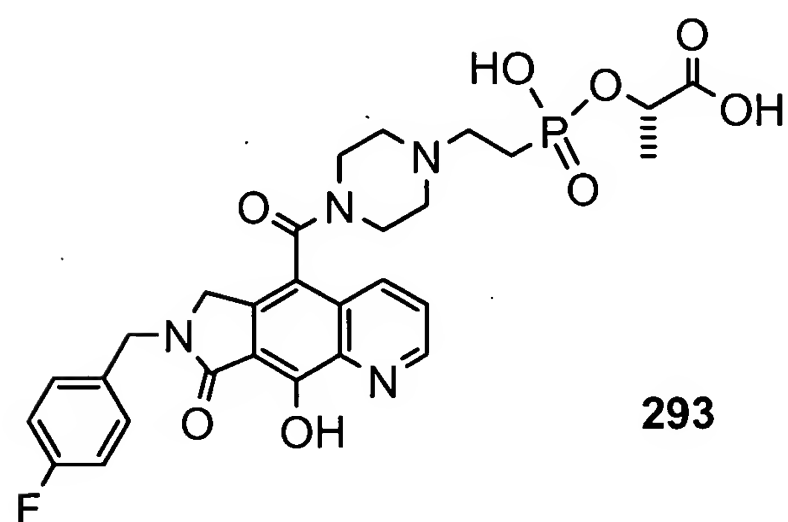
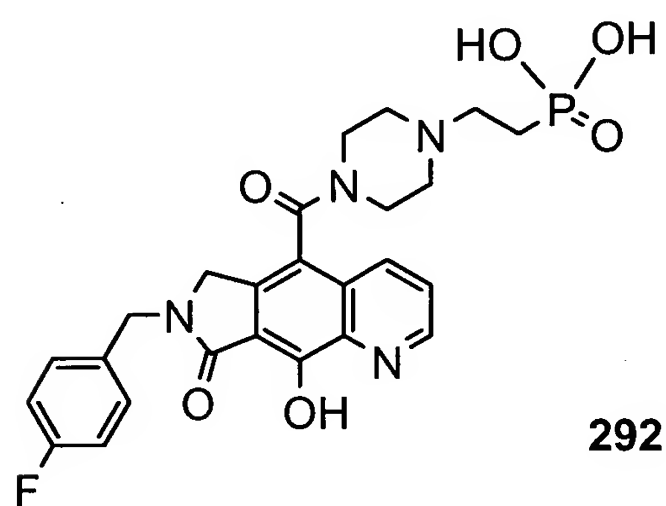
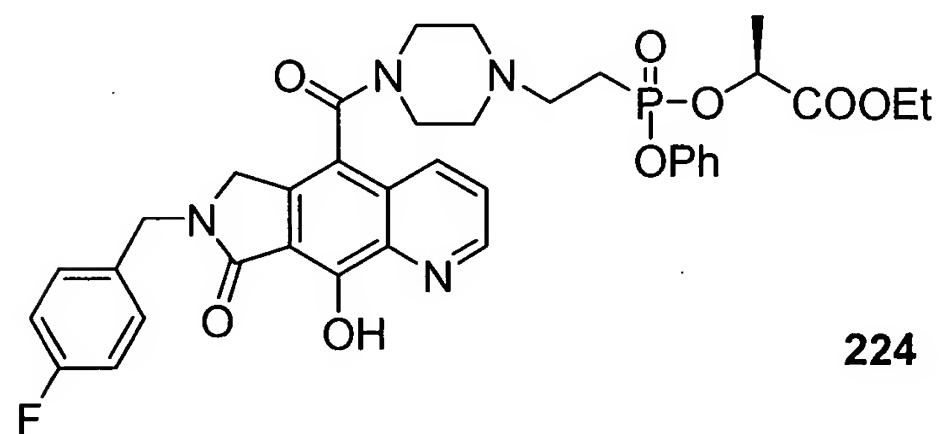
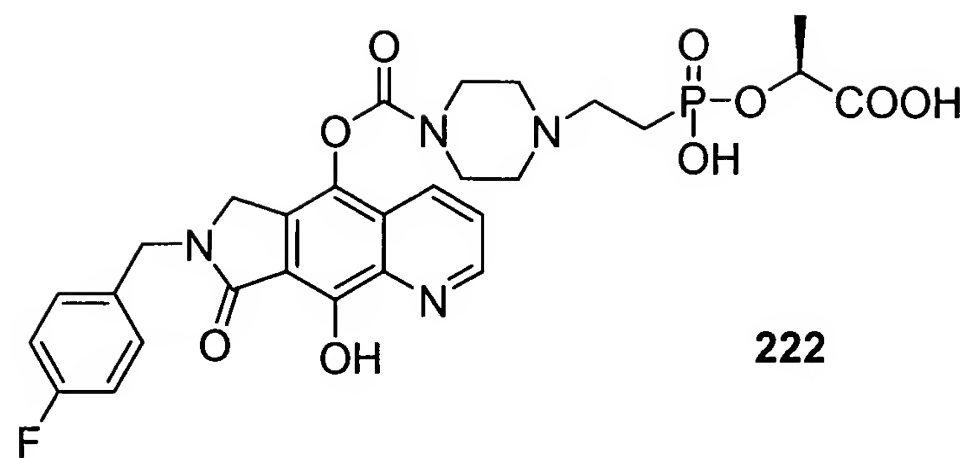
169

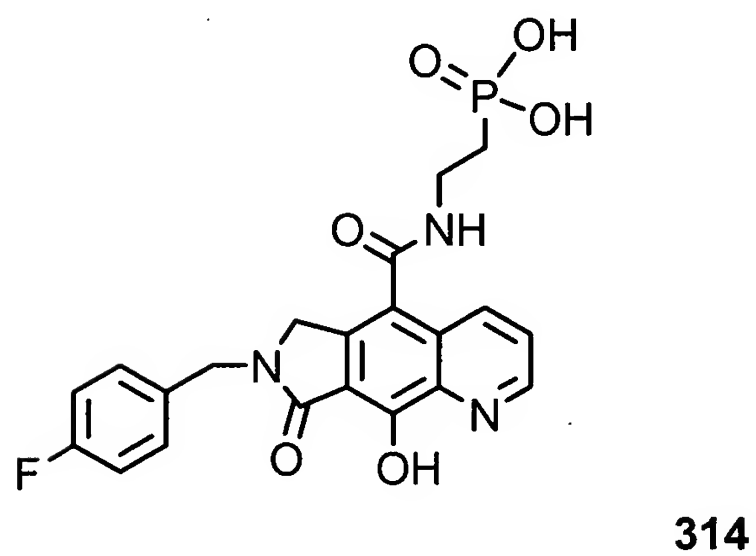
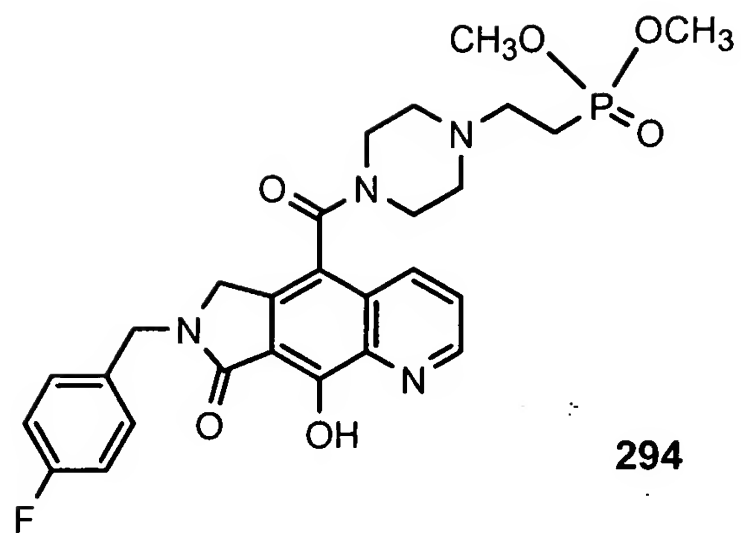


170

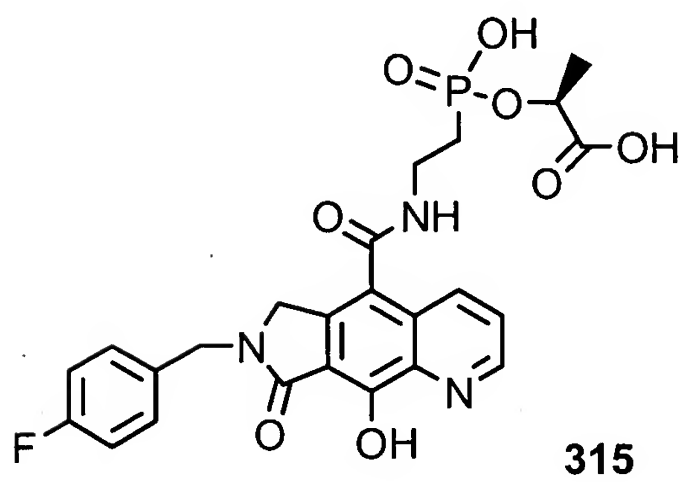




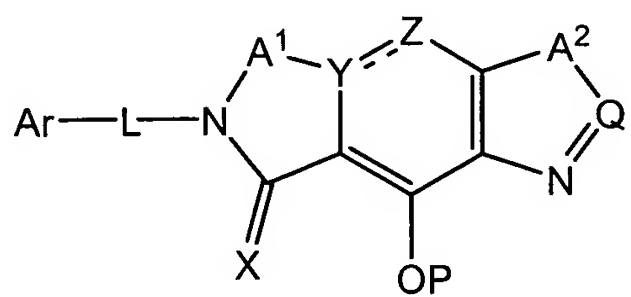




and



49. (once amended): A compound having the structure:



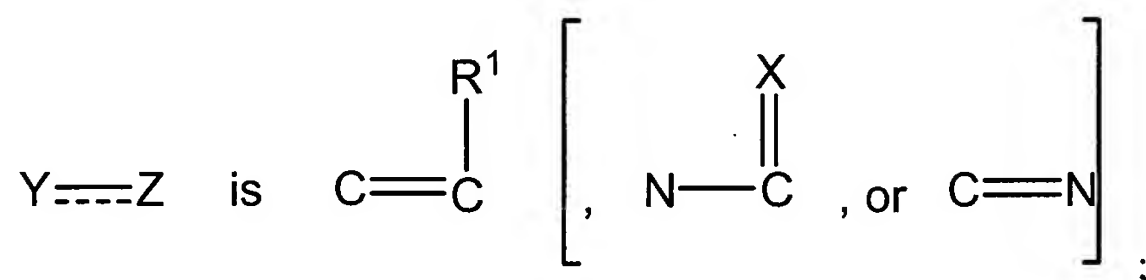
[or a salt thereof;]

wherein:

A^1 [and A^2 are] is independently selected from [O, S, NR,] $C(R^2)_2$, CR^2OR , $CR^2OC(=O)R$, $C(=O)$, $C(=S)$, CR^2SR , and $C(=NR)$,

A^2 is independently selected from $C(R^2)_2-C(R^3)_2$, $C(R^2)=C(R^3)$, $[NR-C(R^3)_2, N=C(R^3), N=N, SO_2-NR,]$ and $C(=O)C(R^3)_2$, $C(=O)NR$, $C(R^2)_2-C(R^3)_2-C(R^3)_2$, $C(R^2)=C(R^3)-C(R^3)_2$, $C(R^2)C(=O)NR$, $C(R^2)C(=S)NR$, $C(R^2)=N-C(R^3)_2$, $C(R^2)=N-NR$, and $N=C(R^3)-NR$];

Q is [N, ^+NR , or] CR^4 ;



L is selected from a bond, O, S, S-S, S(=O), S(=O)₂, S(=O)₂NR, NR, N-OR, C₁-C₁₂ alkylene, C₁-C₁₂ substituted alkylene, C₂-C₁₂ alkenylene, C₂-C₁₂ substituted alkenylene, C₂-C₁₂ alkynylene, C₂-C₁₂ substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), C(=O)NH(CH₂)_n, or (CH₂CH₂O)_n, where n is optionally [may be] 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N-OR, N-NR₂, N-CR₂OR and N-CR₂NR₂;

Ar is selected from (a) a C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

[R¹,] R², R³ and R⁴ are each independently selected from H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate[, and a prodrug moiety];

when taken together on a single carbon, two R² or two R³ may form a spiro ring;

R¹ is independently selected from CR₃, NRSO₂R, OC(=O)NR₂, OC(=O)R, SR, H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

R¹ is independently selected from CR₃, NRSO₂R, OC(=O)OR, OC(=O)NR₂, OC(+O)R, SR, H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

R is independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

R^{X2} is independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

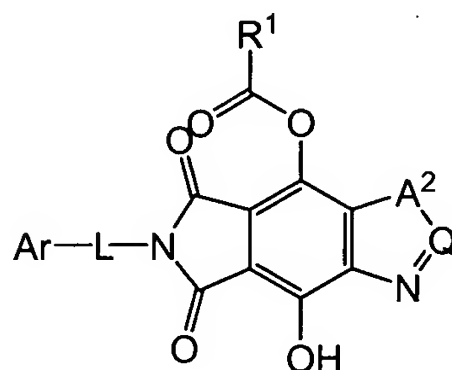
and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof;

with the proviso that when Y=Z is C=C(OH), X is O, A¹ is C(=O), A² is C(R²)=C(R³), and Q is CH, then L is not a bond.

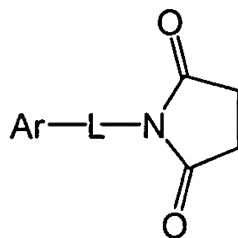
[R is independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate, and a prodrug; and

P is a protecting group selected from benzyhydryl (CHPh₂), trialkylsilyl (R₃Si), 2-trimethylsiloxyethyl, alkoxymethyl (CH₂OR), and ester (C(=O)R)].

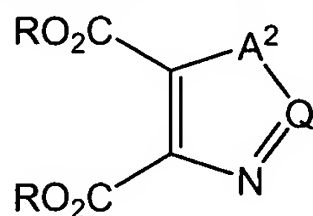
50. (once amended): A process for preparation of a compound having the structure:



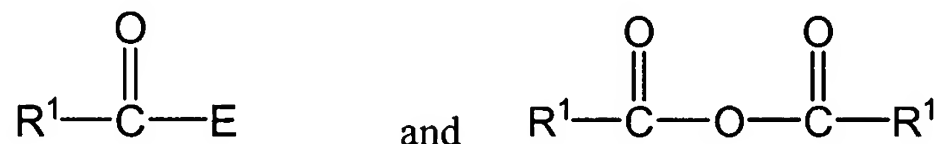
comprising reacting a succinimide compound having the structure:



with a heterocyclic compound having the structure:



and [reaction] reacting with an acylation reagent having [comprising] a formula selected from:



wherein:

A² is selected from [O, S, NR, C(R²)₂, CR²OR, CR²OC(=O)R, C(=O), C(=S), CR²SR, C(=NR),] C(R²)₂-C(R³)₂, C(R²)=C(R³), [NR-C(R³)₂, N=C(R³), N=N, SO₂-NR,] and C(=O)C(R³)₂, [C(=O)NR, C(R²)₂-C(R³)₂-C(R³)₂, C(R²)=C(R³)-C(R³)₂, C(R²)C(=O)NR, C(R²)C(=S)NR, C(R²)=N-C(R³)₂, C(R²)=N-NR, and N=C(R³)-NR];

Q is [N, ⁺NR, or] CR⁴;

L is selected from a bond, O, S, NR, N-OR, C₁-C₁₂ alkyldiyl, C₁-C₁₂ substituted alkyldiyl, C(=O)NH, C(=O), S(=O), S(=O)₂, C(=O)NH(CH₂)_n, and (CH₂CH₂O)_n, where n ranges from 1 to 6;

Ar is selected from (a) a C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

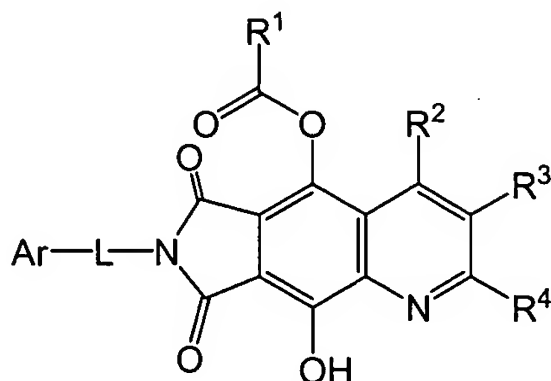
R¹ is selected from R, OR, NR₂, NHR, NHSO₂R, and NRSO₂R;

E is selected from Cl, imidazole, and hydroxybenzotriazole;

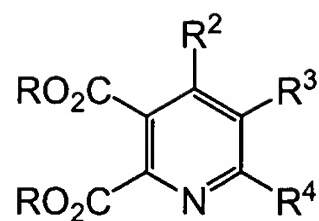
R², R³ and R⁴ are each independently selected from H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

R is selected from C₁-C₆ alkyl, C₁-C₆ substituted alkyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

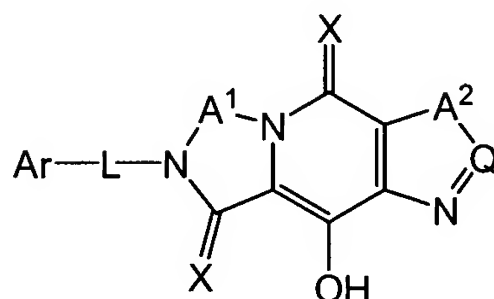
51. (previously presented): The process of claim 50 for preparation of a compound having the structure:



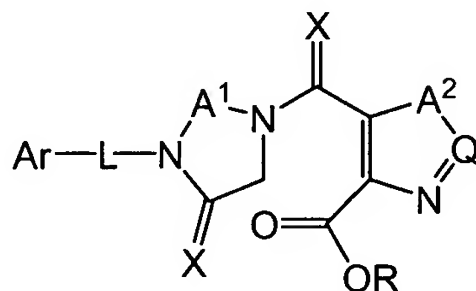
wherein the heterocyclic compound has the structure:



52. (currently amended): A process for preparation of a compound having the structure:



comprising reacting a compound having the structure:



with a basic reagent comprising hydroxide, an alkoxide or an amine;

wherein:

A^1 [and A^2 are] is independently selected from [O, S, NR,] $C(R^2)_2$, CR^2OR , $CR^2OC(=O)R$, $C(=O)$, $C(=S)$, CR^2SR , and $C(=NR)$,

A^2 is independently selected from $C(R^2)_2-C(R^3)_2$, $C(R^2)=C(R^3)$, $[C(R^2)_2-O, NR-C(R^3)_2, N=C(R^3), N=N, SO_2-NR,]$ and $C(=O)C(R^3)_2$, $[C(=O)NR, C(R^2)_2-C(R^3)_2-C(R^3)_2, C(R^2)=C(R^3)-C(R^3)_2, C(R^2)C(=O)NR, C(R^2)C(=S)NR, C(R^2)=N-C(R^3)_2, C(R^2)=N-NR, and N=C(R^3)-NR]$;

Q is [N, ^+NR , or] CR^4 ;

X is selected from O, S, NH, NR, N-OR, N-NR₂, N-CR₂OR and N-CR₂NR₂;

L is selected from a bond, O, S, NR, N-OR, C₁-C₁₂ alkylidyl, C₁-C₁₂ substituted alkylidyl, C(=O)NH, C(=O), S(=O), S(=O)₂, C(=O)NH(CH₂)_n, and (CH₂CH₂O)_n, where n ranges from 1 to 6;

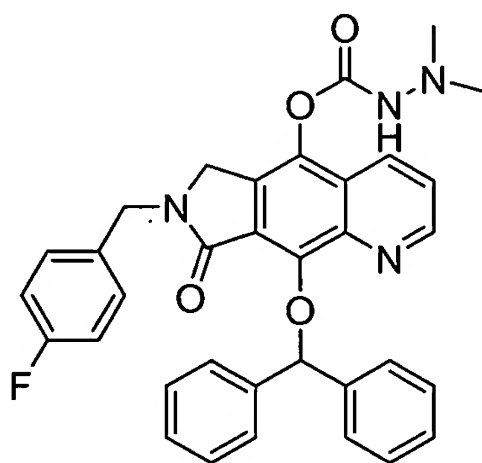
Ar is selected from (a) a C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

R^2 , R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_3-C_{12} carbocycle, C_3-C_{12} substituted carbocycle, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

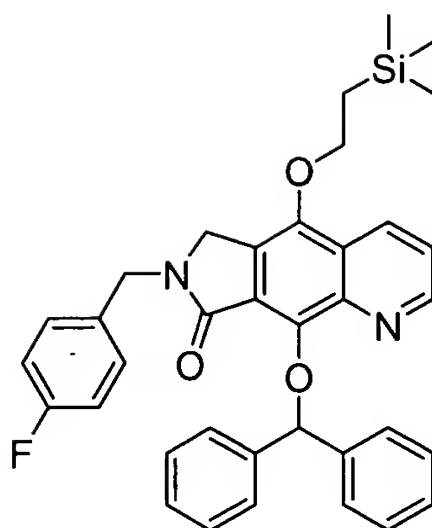
R is selected from C_1-C_6 alkyl, C_1-C_6 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

53. (previously presented): A process for preparation of a compound having structure 115:



115

comprising reacting a compound having the structure 44:



44

with tetrabutylammonium fluoride to form a desilylated intermediate; and reacting the desilylated intermediate with triphosgene (bis(trichloromethyl) carbonate), followed by dimethylhydrazine to form structure 115.

54. (once amended): A compound of claim 1 substituted with [comprising a] phosphonate [prodrug] and capable of accumulating in human PBMC.

55. (previously presented): The compound of claim 54 wherein the intracellular half-life [bioavailability] of the compound or an intracellular metabolite of the compound in human PBMC is increased by at least about 50% [improved] when compared to the analog of the compound not having the phosphonate [or phosphonate prodrug].

56. (canceled)

57. (canceled)

58. (once amended): The compound of claim 55 [56] wherein the half-life is improved by at least about 100%.

59. (canceled)

60. (canceled)

61. (canceled)

62. (canceled)

63. (previously presented): A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

64. (previously presented): The pharmaceutical composition of claim [62] 63 further comprising a therapeutically effective amount of an AIDS treatment agent selected from an HIV inhibitor agent, an anti-infective agent, and an immunomodulator.

65. (previously presented): The pharmaceutical composition of claim 64 wherein the HIV inhibitor agent is an HIV-protease inhibitor.

66. (previously presented): The composition of claim 64 wherein the HIV inhibitor agent is a nucleoside reverse transcriptase inhibitor.

67. (previously presented): The composition of claim 64 wherein the HIV inhibitor agent is a non-nucleoside reverse transcriptase inhibitor.

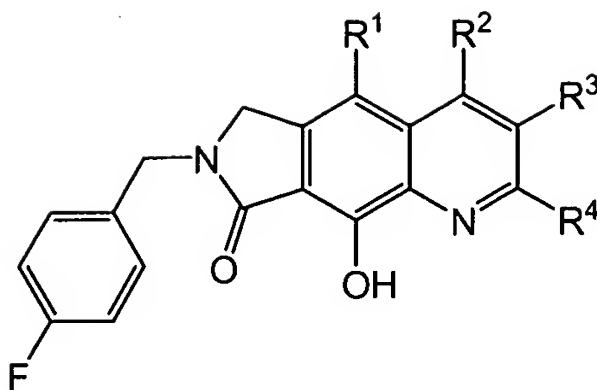
68. (previously presented): A process for making a pharmaceutical composition comprising combining a compound of claim 1 and a pharmaceutically acceptable carrier.

69. (previously presented): A method of inhibiting HIV integrase, comprising the administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

70. (previously presented): A method of treating infection by HIV, or of treating AIDS or ARC, comprising administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

71 – 79 (canceled)

80. (new): A compound having the structure:



wherein R^1 is selected from R, OR, NR_2 , NHR, $NHSO_2R$ and $NRSO_2R$;

R^2 , R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_3-C_{12} carbocycle, C_3-C_{12} substituted carbocycle, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

R is independently selected from H, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof.